# WEST Search History

DATE: Monday, July 28, 2003

| Set Name side by side | Query | Hit Count | Set Name result set |
|---|---|---|---|
| *DB=USPT,PGPB,JPAB,EPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ* | | | |
| L4 | avermectin aglycon | 12 | L4 |
| L3 | avermectin aglycon synthase | 1 | L3 |
| L2 | l1 and (nucleic acid or gene or dna or cdna) | 141 | L2 |
| L1 | avermectin and polyketide synthase | 143 | L1 |

END OF SEARCH HISTORY

WEST

Generate Collection | Print

**Search Results** - Record(s) 1 through 20 of 141 returned.

☐ 1. Document ID: US 20030134398 A1

L2: Entry 1 of 141 File: PGPB Jul 17, 2003

PGPUB-DOCUMENT-NUMBER: 20030134398
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030134398 A1

TITLE: Mitomycin biosynthetic gene cluster

PUBLICATION-DATE: July 17, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Sherman, David H. | St. Louis Park | MN | US | |
| Mao, Yingqing | St. Paul | MN | US | |
| Varoglu, Mustafa | San Diego | CA | US | |
| He, Min | Monsey | NY | US | |
| Sheldon, Paul | St. Paul | MN | US | |

US-CL-CURRENT: 435/119; 435/191, 435/193, 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 2. Document ID: US 20030134313 A1

L2: Entry 2 of 141 File: PGPB Jul 17, 2003

PGPUB-DOCUMENT-NUMBER: 20030134313
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030134313 A1

TITLE: Streptomyces avermitilis gene directing the ratio of B2:B1 avermectins

PUBLICATION-DATE: July 17, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Stutzman-Engwall, Kim J. | East Lyme | CT | US | |
| McArthur, Hamish | Gales Ferry | CT | US | |
| Katoh, Yoshihiro | Aichi | | JP | |

US-CL-CURRENT: 435/6; 435/183, 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 3. Document ID: US 20030129636 A1

L2: Entry 3 of 141 File: PGPB Jul 10, 2003

PGPUB-DOCUMENT-NUMBER: 20030129636
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030129636 A1

TITLE: Streptomyces avermitilis gene directing the ratio of B2:B1 avermectins

PUBLICATION-DATE: July 10, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Stutzman-Engwall, Kim J. | East Lyme | CT | US | |
| McArthur, Hamish | Gales Ferry | CT | US | |
| Katoh, Yoshihiro | Aichi | | JP | |

US-CL-CURRENT: 435/6; 435/183, 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
Draw. Desc | Image

☐ 4. Document ID: US 20030129635 A1

L2: Entry 4 of 141 File: PGPB Jul 10, 2003

PGPUB-DOCUMENT-NUMBER: 20030129635
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030129635 A1

TITLE: Compositions related to Streptomyces avermitilis gene directing the ratio of B2:B1 avermectins

PUBLICATION-DATE: July 10, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Stutzman-Engwall, Kim J. | East Lyme | CT | US | |
| McArthur, Hamish | Gales Ferry | CT | US | |
| Katoh, Yoshihiro | Aichi | | JP | |

US-CL-CURRENT: 435/6; 435/183, 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

☐ 5. Document ID: US 20030124607 A1

L2: Entry 5 of 141 File: PGPB Jul 3, 2003

PGPUB-DOCUMENT-NUMBER: 20030124607
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030124607 A1

TITLE: Methods related to streptomyces avermitilis gene directing the ratio of B2:B1

avermectins

PUBLICATION-DATE: July 3, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Stutzman-Engwall, Kim J. | East Lyme | CT | US | |
| McArthur, Hamish | Gales Ferry | CT | US | |
| Katoh, Yoshihiro | Aichi | | JP | |

US-CL-CURRENT: 435/6; 435/183, 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 6. Document ID: US 20030119018 A1

L2: Entry 6 of 141 File: PGPB Jun 26, 2003

PGPUB-DOCUMENT-NUMBER: 20030119018
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030119018 A1

TITLE: Novel polynucleotides

PUBLICATION-DATE: June 26, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Omura, Satoshi | Tokyo | | JP | |
| Ikeda, Haruo | Kawasaki-shi | | JP | |
| Ishikawa, Jun | Sagamihara-shi | | JP | |
| Horikawa, Hiroshi | Tokyo | | JP | |
| Shiba, Tadayoshi | Tokyo | | JP | |
| Sakaki, Yoshiyuki | Yokohama-shi | | JP | |
| Hattori, Masahira | Tokyo | | JP | |

US-CL-CURRENT: 435/6; 435/252.1, 435/41, 530/350, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 7. Document ID: US 20030114450 A1

L2: Entry 7 of 141 File: PGPB Jun 19, 2003

PGPUB-DOCUMENT-NUMBER: 20030114450
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030114450 A1

TITLE: Benzoquinone ansamycins

PUBLICATION-DATE: June 19, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Santi, Daniel | San Francisco | CA | US | |
| Myles, David C. | Kensington | CA | US | |
| Tian, Zong-Qiang | Fremont | CA | US | |
| Hutchinson, C. Richard | San Mateo | CA | US | |
| Johnson, Robert | Lafayette | CA | US | |
| Zhou, Yi-Qing | Lafayette | CA | US | |
| Feng, Li | Fremont | CA | US | |

US-CL-CURRENT: 514/234.5; 514/252.13, 514/320, 514/337, 514/397, 540/456

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 8. Document ID: US 20030109682 A1

L2: Entry 8 of 141 File: PGPB Jun 12, 2003

PGPUB-DOCUMENT-NUMBER: 20030109682
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030109682 A1

TITLE: Maytansines and maytansine conjugates

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Santi, Daniel | San Francisco | CA | US | |
| Myles, David C. | Kensington | CA | US | |
| Metcalf, Brian | Moraga | CA | US | |
| Hutchinson, C. Richard | San Mateo | CA | US | |
| Ashley, Gary | Alameda | CA | US | |

US-CL-CURRENT: 530/391.1; 540/462

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 9. Document ID: US 20030104597 A1

L2: Entry 9 of 141 File: PGPB Jun 5, 2003

PGPUB-DOCUMENT-NUMBER: 20030104597
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030104597 A1

TITLE: Recombinant narbonolide polyketide synthase

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Ashley, Gary | Alameda | CA | US | |
| Betlach, Melanie C. | San Francisco | CA | US | |
| Betlach, Mary | San Francisco | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |
| Tang, Li | Foster City | CA | US | |

US-CL-CURRENT: 435/193; 435/196, 435/200, 435/252.3, 435/320.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 10. Document ID: US 20030100518 A1

L2: Entry 10 of 141 File: PGPB May 29, 2003

PGPUB-DOCUMENT-NUMBER: 20030100518
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030100518 A1

TITLE: 13-Methyl erythromycin derivatives

PUBLICATION-DATE: May 29, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Wu, Yong-Jin | Madison | CT | US | |
| Su, Wei-Guo | East Lyme | CT | US | |
| Kaneko, Takushi | Guilford | CT | US | |
| Mcarthur, Hamish | Mystic | CT | US | |

US-CL-CURRENT: 514/29; 536/7.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 11. Document ID: US 20030096381 A1

L2: Entry 11 of 141 File: PGPB May 22, 2003

PGPUB-DOCUMENT-NUMBER: 20030096381
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030096381 A1

TITLE: Production of polyketides

PUBLICATION-DATE: May 22, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Julien, Bryan | Oakland | CA | US | |
| Katz, Leonard | Hayward | CA | US | |
| Khosla, Chaitan | Palo Alto | CA | US | |

US-CL-CURRENT: 435/118; 435/193, 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

☐ 12. Document ID: US 20030096374 A1

L2: Entry 12 of 141 File: PGPB May 22, 2003

PGPUB-DOCUMENT-NUMBER: 20030096374
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030096374 A1

TITLE: Synthesis of oligoketides

PUBLICATION-DATE: May 22, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Ashley, Gary | Alameda | CA | US | |
| Chan-Kai, Isaac C. | Hayward | CA | US | |
| Burlingame, Mark A. | San Francisco | CA | US | |

US-CL-CURRENT: 435/74; 536/7.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

☐ 13. Document ID: US 20030092140 A1

L2: Entry 13 of 141 File: PGPB May 15, 2003

PGPUB-DOCUMENT-NUMBER: 20030092140
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030092140 A1

TITLE: Novel polyketides and antibiotics

PUBLICATION-DATE: May 15, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Ashley, Gary | Alameda | CA | US | |
| Chan-Kai, Isaac C. | Hayward | CA | US | |
| Burlingame, Mark A. | San Francisco | CA | US | |

US-CL-CURRENT: 435/130; 435/117, 435/124

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 14. Document ID: US 20030087405 A1

L2: Entry 14 of 141 File: PGPB May 8, 2003

PGPUB-DOCUMENT-NUMBER: 20030087405
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030087405 A1

TITLE: Products encoded by a methymycin/pikromycin biosynthetic gene cluster

PUBLICATION-DATE: May 8, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Sherman, David H. | St. Louis Park | MN | US | |
| Liu, Hung-Wen | Roseville | MN | US | |
| Xue, Yongquan | St. Paul | MN | US | |
| Zhao, Lishan | St. Paul | MN | US | |

US-CL-CURRENT: 435/183; 435/252.3, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 15. Document ID: US 20030082611 A1

L2: Entry 15 of 141 File: PGPB May 1, 2003

PGPUB-DOCUMENT-NUMBER: 20030082611
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030082611 A1

TITLE: Methods and compositions for cellular and metabolic engineering

PUBLICATION-DATE: May 1, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Minshull, Jeremy | Los Altos | CA | US | |
| Stemmer, Willem P.C. | Los Gatos | CA | US | |

US-CL-CURRENT: 435/6; 435/7.1, 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 16. Document ID: US 20030077767 A1

L2: Entry 16 of 141 File: PGPB Apr 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030077767
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030077767 A1

TITLE: Genes and proteins for the biosynthesis of anthramycin

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Farnet, Chris M. | Outremont | | CA | |
| Staffa, Alfredo | Saint-Laurent | | CA | |

US-CL-CURRENT: 435/117; 435/191, 435/252.3, 435/320.1, 435/6, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 17. Document ID: US 20030077760 A1

L2: Entry 17 of 141 File: PGPB Apr 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030077760
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030077760 A1

TITLE: Combinatorial polyketide libraries produced using a modular PKS gene cluster as scaffold

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Palo Alto | CA | US | |
| Ashley, Gary | Alameda | CA | US | |
| Fu, Hong | Fremont | CA | US | |
| Kao, Camilla M. | Palo Alto | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |

US-CL-CURRENT: 435/91.2; 435/76

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 18. Document ID: US 20030077759 A1

L2: Entry 18 of 141 File: PGPB Apr 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030077759
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030077759 A1

TITLE: Plasmids for polyketide production

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Hu, Zhihao | Hayward | CA | US | |
| Hutchinson, Richard C. | Cross Plains | WI | US | |

US-CL-CURRENT: 435/76; 435/252.3, 435/320.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 19. Document ID: US 20030077707 A1

L2: Entry 19 of 141 File: PGPB Apr 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030077707
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030077707 A1

TITLE: Combinatorial polyketide libraries produced using a modular PKS gene cluster as scaffold

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Palo Alto | CA | US | |
| Ashley, Gary | Alameda | CA | US | |
| Fu, Hong | Stanford | CA | US | |
| Kao, Camilla M. | Palo Alto | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |

US-CL-CURRENT: 435/69.1; 435/193, 435/254.2, 435/483

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 20. Document ID: US 20030073824 A1

L2: Entry 20 of 141 File: PGPB Apr 17, 2003

PGPUB-DOCUMENT-NUMBER: 20030073824
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030073824 A1

TITLE: DNA encoding methymycin and pikromycin

PUBLICATION-DATE: April 17, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Sherman, David H. | St. Louis Park | MN | US | |
| Liu, Hung-Wen | Austin | TX | US | |
| Xue, Yongquan | St. Paul | MN | US | |
| Zhao, Lishan | Carlsbad | CA | US | |

US-CL-CURRENT: 536/7.1; 435/252.3, 435/320.1, 435/69.1, 435/75, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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| Terms | Documents |
|---|---|
| l1 and (nucleic acid or gene or dna or cdna) | 141 |

**Display Format:** - Change Format

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**Search Results** - Record(s) 21 through 40 of 141 returned.

☐ 21. Document ID: US 20030073205 A1

L2: Entry 21 of 141 File: PGPB Apr 17, 2003

PGPUB-DOCUMENT-NUMBER: 20030073205
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030073205 A1

TITLE: Production of polyketides

PUBLICATION-DATE: April 17, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Arslanian, Robert L. | Pacifica | CA | US | |
| Ashley, Gary | Alameda | CA | US | |
| Frykman, Scott | Hayward | CA | US | |
| Julien, Bryan | Oakland | CA | US | |
| Katz, Leonard | Oakland | CA | US | |
| Khosla, Chaitan | Palo Alto | CA | US | |
| Lau, Janice | San Mateo | CA | US | |
| Licari, Peter J. | Fremont | CA | US | |
| Regentin, Rika | Hayward | CA | US | |
| Santi, Daniel | San Francisco | CA | US | |
| Tang, Li | Foster City | CA | US | |

US-CL-CURRENT: 435/117; 435/123, 435/252.3, 544/333, 546/148, 546/167, 546/281.7, 548/204

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 22. Document ID: US 20030068677 A1

L2: Entry 22 of 141 File: PGPB Apr 10, 2003

PGPUB-DOCUMENT-NUMBER: 20030068677
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030068677 A1

TITLE: Recombinant production of novel polyketides

PUBLICATION-DATE: April 10, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Palo Alto | CA | US | |
| Kao, Camilla M. | Palo Alto | CA | US | |

US-CL-CURRENT: 435/69.1; 435/193, 435/254.2, 435/320.1, 435/484

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 23. Document ID: US 20030044938 A1

L2: Entry 23 of 141 File: PGPB Mar 6, 2003

PGPUB-DOCUMENT-NUMBER: 20030044938
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030044938 A1

TITLE: Method to produce novel polyketides

PUBLICATION-DATE: March 6, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Stanford | CA | US | |
| Pieper, Rembert | Washington | DC | US | |
| Luo, Guanglin | Madison | CT | US | |
| Cane, David E. | Providence | RI | US | |
| Kao, Camilla | Palo Alto | CA | US | |
| Ashley, Gary | Alameda | CA | US | |

US-CL-CURRENT: 435/76; 435/200, 435/320.1, 435/325, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 24. Document ID: US 20030040084 A1

L2: Entry 24 of 141 File: PGPB Feb 27, 2003

PGPUB-DOCUMENT-NUMBER: 20030040084
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030040084 A1

TITLE: Macrolide analogs

PUBLICATION-DATE: February 27, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Palo Alto | CA | US | |
| Ashley, Gary | Alameda | CA | US | |
| Fu, Hong | Fremont | CA | US | |
| Kao, Camilla M. | Palo Alto | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |

US-CL-CURRENT: 435/76; 435/325, 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 25. Document ID: US 20030027287 A1

L2: Entry 25 of 141 File: PGPB Feb 6, 2003

PGPUB-DOCUMENT-NUMBER: 20030027287
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030027287 A1

TITLE: Recombinant oleandolide polyketide synthase

PUBLICATION-DATE: February 6, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Betlach, Mary C. | San Francisco | CA | US | |
| Shah, Sanjay Krishnakant | Concord | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |
| Tang, Li | Foster City | CA | US | |

US-CL-CURRENT: 435/76; 435/183, 435/320.1, 435/325, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 26. Document ID: US 20030013662 A1

L2: Entry 26 of 141 File: PGPB Jan 16, 2003

PGPUB-DOCUMENT-NUMBER: 20030013662
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030013662 A1

TITLE: Novel polyketide derivatives and recombinant methods for making same

PUBLICATION-DATE: January 16, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Katz, Leonard | Wheeling | IL | US | |
| Stassi, Diane L. | Highland Park | IL | US | |
| Summers, Richard G. JR. | Nashotah | WI | US | |
| Ruan, Xiaoan | Lake Bluff | IL | US | |
| Pereda-Lopez, Ana | Mundelein | IL | US | |
| Kakavas, Stephan J. | Buffalo Grove | IL | US | |

US-CL-CURRENT: 514/28; 536/7.1, 536/7.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 27. Document ID: US 20020192778 A1

L2: Entry 27 of 141 File: PGPB Dec 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020192778
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020192778 A1

TITLE: Genes for the biosynthesis of epothilones

PUBLICATION-DATE: December 19, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Schupp, Thomas | Mohlin | NC | CH | |
| Ligon, James Madison | Apex | NC | US | |
| Molnar, Istvan | Durham | NC | US | |
| Zirkle, Ross | Raleigh | NC | US | |
| Cyr, Devon Dawn | Fuquay-Varina | NC | US | |
| Gorlach, Jorn | Durham | | US | |

US-CL-CURRENT: 435/183; 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 28. Document ID: US 20020192767 A1

L2: Entry 28 of 141 File: PGPB Dec 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020192767
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020192767 A1

TITLE: Biosynthesis of polyketide synthase substrates

PUBLICATION-DATE: December 19, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Palo Alto | CA | US | |
| Pfeifer, Blaine | Palo Alto | CA | US | |

US-CL-CURRENT: 435/76; 435/119, 435/252.3, 435/252.33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 29. Document ID: US 20020173008 A1

L2: Entry 29 of 141 File: PGPB Nov 21, 2002

PGPUB-DOCUMENT-NUMBER: 20020173008
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020173008 A1

TITLE: Recombinant polyketide synthase genes

PUBLICATION-DATE: November 21, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Hu, Zhihao | Hayward | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |
| Santi, Daniel V. | San Francisco | CA | US | |

US-CL-CURRENT: 435/76; 435/193, 435/253.5, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 30. Document ID: US 20020168730 A1

L2: Entry 30 of 141 File: PGPB Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020168730
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020168730 A1

TITLE: Production of 8,8a-dihydroxy-6-deoxyerythronolide B

PUBLICATION-DATE: November 14, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| McDaniel, Robert | Palo Alto | CA | US | |

US-CL-CURRENT: 435/75; 435/252.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 31. Document ID: US 20020164742 A1

L2: Entry 31 of 141 File: PGPB Nov 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020164742
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020164742 A1

TITLE: DNA encoding methymycin and pikromycin

PUBLICATION-DATE: November 7, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Sherman, David H. | St. Louis Park | MN | US | |
| Liu, Hung-Wen | Roseville | MN | US | |
| Xue, Yongquan | St. Paul | MN | US | |
| Zhao, Lishan | St. Paul | MN | US | |

US-CL-CURRENT: 435/191; 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 32. Document ID: US 20020142401 A1

L2: Entry 32 of 141 File: PGPB Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020142401
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020142401 A1

TITLE: Isolated gene for methylmalonyl CoA epimerase and uses thereof

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Santi, Daniel | San Francisco | CA | US | |
| Dayem, Linda | Belmont | CA | US | |
| Kealey, James | San Rafael | CA | US | |

US-CL-CURRENT: 435/76; 435/252.3, 435/320.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 33. Document ID: US 20020142400 A1

L2: Entry 33 of 141 File: PGPB Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020142400
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020142400 A1

TITLE: Production of polyketides in bacteria and yeast

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Barr, Philip J. | Oakland | CA | US | |
| Santi, Daniel V. | San Francisco | CA | US | |
| Ashley, Gary W. | Alameda | CA | US | |
| Ziermann, Rainer | San Mateo | CA | US | |

US-CL-CURRENT: 435/76; 435/193, 435/252.33, 435/254.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 34. Document ID: US 20020128213 A1

L2: Entry 34 of 141 File: PGPB Sep 12, 2002

PGPUB-DOCUMENT-NUMBER: 20020128213
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020128213 A1

TITLE: Sixteen-membered macrolide compounds

PUBLICATION-DATE: September 12, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Katz, Leonard | Oakland | CA | US | |
| Ashley, Gary | Alameda | CA | US | |
| Burlingame, Mark A. | San Francisco | CA | US | |
| Dong, Steven D. | San Francisco | CA | US | |
| Fu, Hong | Union City | CA | US | |
| Li, Yong | Palo Alto | CA | US | |
| Myles, David C. | Kensington | CA | US | |

US-CL-CURRENT: 514/30; 536/7.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 35. Document ID: US 20020111317 A1

L2: Entry 35 of 141 File: PGPB Aug 15, 2002

PGPUB-DOCUMENT-NUMBER: 20020111317
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020111317 A1

TITLE: Sixteen-membered macrolide compounds

PUBLICATION-DATE: August 15, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Katz, Leonard | Oakland | CA | US | |
| Ashley, Gary | Alameda | CA | US | |

US-CL-CURRENT: 514/28; 536/7.1, 536/7.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 36. Document ID: US 20020110897 A1

L2: Entry 36 of 141 File: PGPB Aug 15, 2002

PGPUB-DOCUMENT-NUMBER: 20020110897
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020110897 A1

TITLE: Polyketide synthase encoded by a methymycin/pikromycin biosynthetic gene cluster

PUBLICATION-DATE: August 15, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Sherman, David H. | St. Louis Park | MN | US | |
| Liu, Hung-Wen | Roseville | MN | US | |
| Xue, Yongquan | St. Paul | MN | US | |
| Zhao, Lishan | St. Paul | MN | US | |

US-CL-CURRENT: 435/252.3; 435/320.1, 435/69.1, 536/23.7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 37. Document ID: US 20020110874 A1

L2: Entry 37 of 141 File: PGPB Aug 15, 2002

PGPUB-DOCUMENT-NUMBER: 20020110874
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020110874 A1

TITLE: Recombinant production of novel polyketides

PUBLICATION-DATE: August 15, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Stanford | CA | US | |
| Hopwood, David A. | Norwich | CA | GB | |
| Ebert-Khosla, Susanne | Stanford | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |
| Fu, Hong | Stanford | CA | US | |
| Kao, Camilla | Stanford | | US | |

US-CL-CURRENT: 435/76; 435/252.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 38. Document ID: US 20020068332 A1

L2: Entry 38 of 141 File: PGPB Jun 6, 2002

PGPUB-DOCUMENT-NUMBER: 20020068332
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020068332 A1

TITLE: Macrolide analogs

PUBLICATION-DATE: June 6, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Palo Alto | CA | US | |
| Ashley, Gary | Alameda | CA | US | |
| Fu, Hong | Fremont | CA | US | |
| Kao, Camilla M. | Palo Alto | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |

US-CL-CURRENT: 435/76; 435/325, 435/91.2, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 39. Document ID: US 20020052028 A1

L2: Entry 39 of 141 File: PGPB May 2, 2002

PGPUB-DOCUMENT-NUMBER: 20020052028
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020052028 A1

TITLE: Bio-intermediates for use in the chemical synthesis of polyketides

PUBLICATION-DATE: May 2, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Santi, Daniel | San Francisco | CA | US | |
| Ashley, Gary | Alameda | CA | US | |
| Myles, David C. | Kensington | CA | US | |

US-CL-CURRENT: 435/76; 435/118

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 40. Document ID: US 20020051998 A1

L2: Entry 40 of 141 File: PGPB May 2, 2002

PGPUB-DOCUMENT-NUMBER: 20020051998
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020051998 A1

TITLE: Directed evolution of biosynthetic and biodegradation pathways

PUBLICATION-DATE: May 2, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Schmidt-Dannert, Claudia | Shoreview | MN | US | |
| Arnold, Frances H. | Pasadena | CA | US | |

US-CL-CURRENT: 435/7.1; 435/325, 435/410, 435/67

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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| Terms | Documents |
|---|---|
| l1 and (nucleic acid or gene or dna or cdna) | 141 |

**Display Format:** - Change Format

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**Search Results** - Record(s) 41 through 60 of 141 returned.

☐ 41. Document ID: US 20020045220 A1

L2: Entry 41 of 141 File: PGPB Apr 18, 2002

PGPUB-DOCUMENT-NUMBER: 20020045220
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020045220 A1

TITLE: Biosynthesis of polyketide synthase substrates

PUBLICATION-DATE: April 18, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Palo Alto | CA | US | |
| Pfeifer, Blaine | Stan Ford | CA | US | |

US-CL-CURRENT: 435/76; 435/252.3, 435/252.33, 536/7.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 42. Document ID: US 20020045177 A1

L2: Entry 42 of 141 File: PGPB Apr 18, 2002

PGPUB-DOCUMENT-NUMBER: 20020045177
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020045177 A1

TITLE: Microorganism genomics, compositions and methods related thereto

PUBLICATION-DATE: April 18, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Handelsman, Jo | Madison | WI | US | |
| Goodman, Robert M. | Madison | WI | US | |
| Rondon, Michelle R. | Madison | WI | US | |

US-CL-CURRENT: 435/6; 435/29, 435/320.1, 435/41

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 43. Document ID: US 20020034797 A1

L2: Entry 43 of 141 File: PGPB Mar 21, 2002

PGPUB-DOCUMENT-NUMBER: 20020034797
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020034797 A1

TITLE: MODIFIED MODULAR PKS WITH RETAINED SCAFFOLD

PUBLICATION-DATE: March 21, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| KHOSLA, CHAITAN | STANFORD | CA | US | |
| ASHLEY, GARY | ALAMEDA | CA | US | |
| FU, HONG | STANFORD | CA | US | |
| KAO, CAMILLA M. | STANFORD | CA | US | |
| MCDANIEL, ROBERT | PALO ALTO | CA | US | |

US-CL-CURRENT: 435/183; 435/252.35, 435/320.1, 435/7.6, 435/91.4, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 44. Document ID: US 20020028444 A1

L2: Entry 44 of 141 File: PGPB Mar 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020028444
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020028444 A1

TITLE: METHOD AND KITS FOR PREPARING MULTICOMPONENT NUCLEIC ACID CONSTRUCTS

PUBLICATION-DATE: March 7, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| HARNEY, PETER D. | ALISO VIEJO | CA | US | |
| HARNEY, JENNIFER | ALISO VIEJO | CA | US | |

US-CL-CURRENT: 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 45. Document ID: US 20020025517 A1

L2: Entry 45 of 141 File: PGPB Feb 28, 2002

PGPUB-DOCUMENT-NUMBER: 20020025517
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020025517 A1

TITLE: METHODS AND COMPOSITIONS FOR CELLULAR AND METABOLIC ENGINEERING

PUBLICATION-DATE: February 28, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| MINSHULL, JEREMY | SAN FRANCISCO | CA | US | |
| STEMMER, WILLEM P. C. | LOS GATOS | CA | US | |

US-CL-CURRENT: 435/6; 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 46. Document ID: US 20020010328 A1

L2: Entry 46 of 141 File: PGPB Jan 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020010328
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020010328 A1

TITLE: Polyketide synthase enzymes and recombinant DNA constructs therefor

PUBLICATION-DATE: January 24, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Reeves, Christopher | Orinda | CA | US | |
| Chu, Daniel | Santa Clara | CA | US | |
| Khosla, Chaitan | Palo Alto | CA | US | |
| Santi, Daniel | San Francisco | CA | US | |
| Wu, Kai | Foster City | CA | US | |

US-CL-CURRENT: 540/456; 435/183, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 47. Document ID: US 20020004487 A1

L2: Entry 47 of 141 File: PGPB Jan 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020004487
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020004487 A1

TITLE: Novel erythromycins and process for their preparation

PUBLICATION-DATE: January 10, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Leadlay, Peter Francis | Cambridge | | GB | |
| Staunton, James | Cambridge | | GB | |
| Cortes, Jesus | Cambridge | | GB | |
| Pacey, Michael Stephen | Broadstairs | | GB | |

US-CL-CURRENT: 514/29; 536/7.2, 536/7.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 48. Document ID: US 20020004229 A1

L2: Entry 48 of 141 File: PGPB Jan 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020004229
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020004229 A1

TITLE: Overproduction hosts for biosynthesis of polyketides

PUBLICATION-DATE: January 10, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Santi, Daniel | San Francisco | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |
| Tang, Li | Foster City | CA | US | |
| Khosla, Chaitan | Palo Alto | CA | US | |

US-CL-CURRENT: 435/76; 435/254.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 49. Document ID: US 20020002712 A1

L2: Entry 49 of 141 File: PGPB Jan 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020002712
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020002712 A1

TITLE: Production of polyketides in plants

PUBLICATION-DATE: January 3, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Betlach, Mary C. | San Francisco | CA | US | |
| Kealey, James T. | Davis | CA | US | |
| Gutterson, Neal | Oakland | CA | US | |
| Ralston, Ed | Pleasant Hill | CA | US | |

US-CL-CURRENT: 800/278; 435/419, 435/69.7, 536/23.74, 800/288, 800/298

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 50. Document ID: US 20010039021 A1

L2: Entry 50 of 141 File: PGPB Nov 8, 2001

PGPUB-DOCUMENT-NUMBER: 20010039021
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010039021 A1

TITLE: Recombinant production of novel

PUBLICATION-DATE: November 8, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Stanford | CA | US | |
| Hopwood, David A. | Norwich | CA | GB | |
| Ebert-Khosla, Suzanne | Stanford | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |
| Fu, Hong | Stanford | CA | US | |
| Kao, Camilla | Stanford | | US | |

US-CL-CURRENT: 435/7.1; 435/76

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 51. Document ID: US 20010034046 A1

L2: Entry 51 of 141 File: PGPB Oct 25, 2001

PGPUB-DOCUMENT-NUMBER: 20010034046
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010034046 A1

TITLE: Production of 8,8a-dihydroxy-6-deoxyerythronolide B

PUBLICATION-DATE: October 25, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| McDaniel, Robert | Palo Alto | CA | US | |

US-CL-CURRENT: 435/76; 536/7.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 52. Document ID: US 20010024818 A1

L2: Entry 52 of 141 File: PGPB Sep 27, 2001

PGPUB-DOCUMENT-NUMBER: 20010024818
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010024818 A1

TITLE: Streptomyces avermitilis gene directing the ratio of B2:B1 avermectins

PUBLICATION-DATE: September 27, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Stutzman-Engwall, Kim J. | East Lyme | CT | US | |
| McArthur, Hamish | Gales Ferry | CT | US | |
| Katoh, Yoshihiro | Aichi | | JP | |

US-CL-CURRENT: 435/253.5; 435/183, 435/69.1, 435/76, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 53. Document ID: US 20010024811 A1

L2: Entry 53 of 141 File: PGPB Sep 27, 2001

PGPUB-DOCUMENT-NUMBER: 20010024811
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010024811 A1

TITLE: Method to produce novel polyketides

PUBLICATION-DATE: September 27, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Stanford | CA | US | |
| Pieper, Rembert | Washington | DC | US | |
| Luo, Guanglin | Madison | CT | US | |
| Crane, David E. | Providence | RI | US | |
| Kao, Camilla | Palo Alto | CA | US | |

US-CL-CURRENT: 435/91.4; 435/118, 435/124, 435/91.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 54. Document ID: US 20010024810 A1

L2: Entry 54 of 141 File: PGPB Sep 27, 2001

PGPUB-DOCUMENT-NUMBER: 20010024810
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010024810 A1

TITLE: Method to prepare macrolide analogs

PUBLICATION-DATE: September 27, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Khosla, Chaitan | Stanford | CA | US | |
| Ashley, Gary | Alameda | CA | US | |
| Fu, Hong | Stanford | CA | US | |
| Kao, Camilla M. | Stanford | CA | US | |
| McDaniel, Robert | Palo Alto | CA | US | |

US-CL-CURRENT: 435/91.1; 435/148, 435/183

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 55. Document ID: US 20010016598 A1

L2: Entry 55 of 141 File: PGPB Aug 23, 2001

PGPUB-DOCUMENT-NUMBER: 20010016598
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010016598 A1

TITLE: ERYTHROMYCINS AND PROCESS FOR THEIR PREPARATION

PUBLICATION-DATE: August 23, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| LEADLAY, PETER FRANCIS | CAMBRIDGE | | GB | |
| STAUNTON, JAMES | CAMBRIDGE | | GB | |
| CORTES, JESUS | CAMBRIDGE | | GB | |
| PACEY, MICHAEL STEPHEN | BROADSTAIRS | | GB | |

US-CL-CURRENT: 514/450

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 56. Document ID: US 20010016350 A1

L2: Entry 56 of 141 File: PGPB Aug 23, 2001

PGPUB-DOCUMENT-NUMBER: 20010016350
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010016350 A1

TITLE: Streptomyces avermitilis gene directing the ratio of B2:B1 avermectins

PUBLICATION-DATE: August 23, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Stutzman-Engwall, Kim J. | East Lyme | CT | US | |
| McArthur, Hamish | Gales Ferry | CT | US | |
| Katoh, Yoshihiro | Aichi | | JP | |

US-CL-CURRENT: 435/253.5; 435/320.1, 435/476, 536/23.7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 57. Document ID: US 6583290 B1

L2: Entry 57 of 141 File: USPT Jun 24, 2003

US-PAT-NO: 6583290
DOCUMENT-IDENTIFIER: US 6583290 B1

TITLE: 14-methyl epothilone derivatives

DATE-ISSUED: June 24, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Julien; Bryan | Oakland | CA | | |
| Katz; Leonard | Hayward | CA | | |
| Khosla; Chaitan | Palo Alto | CA | | |
| Tang; Li | Foster City | CA | | |
| Ziermann; Rainer | San Mateo | CA | | |

US-CL-CURRENT: 548/203; 181/205, 546/268.1

ABSTRACT:

Compounds of the invention include 14-mehtyl epothilone derivatives. More generally, preferred compounds of the invention are those that can be produced by altering the epothilone PKS genes as described herein and optionally by action of epothilone modification enzymes and/or by chemically modifying the resulting epothilones produces when those genes are expressed.

2 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 58. Document ID: US 6558942 B1

L2: Entry 58 of 141 File: USPT May 6, 2003

US-PAT-NO: 6558942
DOCUMENT-IDENTIFIER: US 6558942 B1

TITLE: Combinatorial polyketide libraries produced using a modular PKS gene cluster as scaffold

DATE-ISSUED: May 6, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Palo Alto | CA | | |
| Kao; Camilla M. | Palo Alto | CA | | |

US-CL-CURRENT: 435/253.5; 435/4, 435/41, 435/76, 514/29, 536/7.1

ABSTRACT:

Combinatorial libraries of polyketides can be obtained by suitable manipulation of a host modular polyketide synthase gene cluster such as that which encodes the PKS for

erythromycin. The combinatorial library is useful as a source of pharmaceutically active compounds. In addition, novel polyketides and antibiotics are prepared using this method.

53 Claims, 24 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 22

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 59. Document ID: US 6531299 B1

L2: Entry 59 of 141 File: USPT Mar 11, 2003

US-PAT-NO: 6531299
DOCUMENT-IDENTIFIER: US 6531299 B1

TITLE: Cell-free synthesis of polyketides

DATE-ISSUED: March 11, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Pieper; Rembert | Washington | DC | | |
| Luo; Guanglin | Providence | RI | | |
| Cane; David E. | Providence | RI | | |

US-CL-CURRENT: 435/75; 435/76, 435/77, 435/78, 435/79, 435/80, 435/81, 435/82, 435/83

ABSTRACT:

Cell-free systems which effect the production of polyketides employing modular polyketide synthases are described. Libraries of new and/or known polyketides may also be produced in cell-free systems employing aromatic PKS, modular PKS or both.

15 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 60. Document ID: US 6524841 B1

L2: Entry 60 of 141 File: USPT Feb 25, 2003

US-PAT-NO: 6524841
DOCUMENT-IDENTIFIER: US 6524841 B1

TITLE: Recombinant megalomicin biosynthetic genes and uses thereof

DATE-ISSUED: February 25, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| McDaniel; Robert | Palo Alto | CA | | |
| Volchegursky; Yanina | Emeryville | CA | | |

US-CL-CURRENT: 435/252.3; 435/252.35, 435/254.11, 435/320.1, 435/325, 435/419, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Recombinant nucleic acids that encode all or a portion of the megAI gene of the megalomicin polyketide synthase (PKS) of Micromonospora megalomicea are used to produce recombinant PKS enzymes in host cells to make megalomicin, megalomicin derivatives, and other polyketides that are useful as antibiotics, motilides, and antiparasitics.

7 Claims, 70 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 70

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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| Terms | Documents |
|---|---|
| l1 and (nucleic acid or gene or dna or cdna) | 141 |

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☐ 61. Document ID: US 6521406 B1

L2: Entry 61 of 141 File: USPT Feb 18, 2003

US-PAT-NO: 6521406
DOCUMENT-IDENTIFIER: US 6521406 B1

TITLE: SpnG, a gene for spinosyn insecticide biosynthesis

DATE-ISSUED: February 18, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Baltz; Richard H. | Indianapolis | IN | | |
| Broughton; M. Christine | Indianapolis | IN | | |
| Crawford; Kathryn P. | Indianapolis | IN | | |
| Madduri; Krishnamurthy | Woodlawn | OH | | |
| Merlo; Donald J. | Carmel | IN | | |
| Treadway; Patti J. | Greenwood | IN | | |
| Turner; Jan R. | Carmel | IN | | |
| Waldron; Clive | Indianapolis | IN | | |

US-CL-CURRENT: 435/6; 435/252.3, 435/254.11, 435/320.1, 435/325, 435/419, 536/23.2

ABSTRACT:

Spinosyn biosynthetic genes from Saccharopolyspora spinosa, spinosyn producing microorganisms transformed with the biosynthetic genes, methods using the biosynthetic genes to increase production of spinosyn insecticidal macrolides, and methods using the genes or fragments thereof to change the products produced by spinosyn-producing microorganisms are provided.

6 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 62. Document ID: US 6511841 B2

L2: Entry 62 of 141 File: USPT Jan 28, 2003

US-PAT-NO: 6511841
DOCUMENT-IDENTIFIER: US 6511841 B2

TITLE: Streptomyces avermitilis gene directing the ratio of B2:B1 avermectins

DATE-ISSUED: January 28, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Stutzman-Engwall; Kim J. | East Lyme | CT | | |
| McArthur; Hamish | Gales Ferry | CT | | |
| Katoh; Yoshihiro | Aichi | | | JP |

US-CL-CURRENT: 435/253.5; 435/119, 435/252.3, 435/252.35, 435/320.1, 435/440, 435/471, 435/476, 435/486, 435/70.1, 435/75, 435/76, 530/350, 536/23.1, 536/23.7, 536/23.74, 536/7.1

ABSTRACT:

The present invention relates to polynucleotide molecules comprising nucleotide sequences encoding an aveC gene product, which polynucleotide molecules can be used to alter the ratio or amount of class 2:1 avermectins produced in fermentation cultures of S. avermitilis. The present invention further relates to vectors, host cells, and mutant strains of S. avermitilis in which the aveC gene has been inactivated, or mutated so as to change the ratio or amount of class 2:1 avermectins produced.

18 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 63. Document ID: US 6509455 B1

L2: Entry 63 of 141 File: USPT Jan 21, 2003

US-PAT-NO: 6509455
DOCUMENT-IDENTIFIER: US 6509455 B1

TITLE: Recombinant narbonolide polyketide synthase

DATE-ISSUED: January 21, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ashley; Gary | Alameda | CA | | |
| Betlach; Melanie C. | Burlingame | CA | | |
| Betlach; Mary | San Francisco | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Tang; Li | Foster City | CA | | |

US-CL-CURRENT: 536/23.2; 435/193, 435/320.1, 536/23.7

ABSTRACT:

Recombinant DNA compounds that encode all or a portion of the narbonolide polyketide synthase are used to express recombinant polyketide synthase genes in host cells for the production of narbonolide, narbonolide derivatives, and polyketides that are useful as antibiotics and as intermediates in the synthesis of compounds with pharmaceutical value.

2 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 64. Document ID: US 6509159 B2

L2: Entry 64 of 141 File: USPT Jan 21, 2003

US-PAT-NO: 6509159
DOCUMENT-IDENTIFIER: US 6509159 B2

TITLE: Methods related to Streptomyces avermitilis gene directing the ratio of B2:B1 avermectins

DATE-ISSUED: January 21, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Stutzman-Engwall; Kim J. | East Lyme | CT | | |
| McArthur; Hamish | Gales Ferry | CT | | |
| Katoh; Yoshihiro | Aichi | | | JP |

US-CL-CURRENT: 435/6; 435/76

ABSTRACT:

The present invention relates to polynucleotide molecules comprising nucleotide sequences encoding the aveC gene product, which polynucleotide molecules can be used to alter the ratio or amount of class 2:1 avermectins produced in fermentation cultures of Streptomyces avermitilis. The present invention further relates to vectors, host cells, and mutant strains of Streptomyces avermitilis in which the aveC gene has been inactivated, or mutated so as to change the ratio or amount of class 2:1 avermectins produced.

2 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 65. Document ID: US 6503741 B1

L2: Entry 65 of 141 File: USPT Jan 7, 2003

US-PAT-NO: 6503741
DOCUMENT-IDENTIFIER: US 6503741 B1

TITLE: Polyketide synthase genes from Streptomyces venezuelae

DATE-ISSUED: January 7, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ashley; Gary | Alameda | CA | | |
| Betlach; Melanie C. | Burlingame | CA | | |
| Betlach; Mary | San Francisco | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Tang; Li | Foster City | CA | | |

US-CL-CURRENT: 435/183; 435/189, 435/193, 435/232, 435/252.33, 435/252.35, 435/254.2, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Combinatorial libraries of polyketides can be obtained by suitable manipulation of a host modular polyketide synthase gene cluster such as that which encodes the PKS for picromycin. The combinatorial library is useful as a source of pharmaceutically active compounds. In addition, novel polyketides and antibiotics are prepared using this method.

16 Claims, 37 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 30



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☐ 66. Document ID: US 6503737 B1

L2: Entry 66 of 141 File: USPT Jan 7, 2003

US-PAT-NO: 6503737
DOCUMENT-IDENTIFIER: US 6503737 B1

TITLE: Isolated nucleic acids relating to the fkbA gene within the FK-520 polyketide synthase gene cluster

DATE-ISSUED: January 7, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Reeves; Christopher | Orinda | CA | | |
| Chu; Daniel | Santa Clara | CA | | |
| Khosla; Chaitan | Palo Alto | CA | | |
| Santi; Daniel | San Francisco | CA | | |
| Wu; Kai | Foster City | CA | | |

US-CL-CURRENT: 435/76; 435/252.3, 435/252.35, 435/320.1, 536/23.1, 536/23.2

ABSTRACT:

Host cells comprising recombinant vectors encoding the FK-520 polyketide synthase and FK-520 modification enzymes can be used to produce the FK-520 polyketide. Recombinant DNA constructs comprising one or more FK-520 polyketide synthase domains, modules, open reading frames, and variants thereof can be used to produce recombinant polyketide synthases and a variety of different polyketides with application as pharmaceutical and veterinary products.

34 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 67. Document ID: US 6500960 B1

L2: Entry 67 of 141 File: USPT Dec 31, 2002

US-PAT-NO: 6500960
DOCUMENT-IDENTIFIER: US 6500960 B1

TITLE: Method to produce novel polyketides

DATE-ISSUED: December 31, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Pieper; Rembert | Washington | DC | | |
| Luo; Guanglin | Madison | CT | | |
| Cane; David E. | Providence | RI | | |
| Kao; Camilla | Palo Alto | CA | | |

US-CL-CURRENT: 549/264

ABSTRACT:

Modified PKS gene clusters which produce novel polyketides in an efficient system in a host cell or in a cell free extract are described. The novel polyketides result from the incorporation of diketides of the formula ##STR1##

wherein A is a moiety that activates the diketide, and at least one of R.sup.1 and R.sup.2 is a substituent other than that natively occurring in the diketide normally processed by the modified PKS cluster. The polyketides may also be glycosylated to provide antibiotics.

17 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 68. Document ID: US 6495318 B2

L2: Entry 68 of 141 File: USPT Dec 17, 2002

US-PAT-NO: 6495318
DOCUMENT-IDENTIFIER: US 6495318 B2

TITLE: Method and kits for preparing multicomponent nucleic acid constructs

DATE-ISSUED: December 17, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Harney; Peter D. | late of Aliso Viejo | CA | | |

US-CL-CURRENT: 435/6; 435/254.2, 435/320.1, 435/91.1, 435/91.2, 536/22.1, 536/24.3, 536/24.33, 536/24.5

ABSTRACT:

The invention provides a highly efficient, rapid, and cost effective method of linking nucleic acid components in a predetermined order to produce a nucleic acid multicomponent construct. The invention further provides nucleic acid components, each nucleic acid component comprising a double stranded nucleic acid molecule having at least one single stranded 5' or 3' terminal sequence, the terminal sequence having sufficient complementarity to either a terminal sequence in a separate nucleic acid component or to a sequence in a linking nucleic acid molecule so as to allow for specific annealing of complementary sequences and linkage of the components in a predetermined order. Kits containing reagents required to practice the method of the invention are also provided.

43 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5



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☐ 69. Document ID: US 6492562 B1

L2: Entry 69 of 141 File: USPT Dec 10, 2002

US-PAT-NO: 6492562
DOCUMENT-IDENTIFIER: US 6492562 B1

TITLE: Racemic thioesters for production of polyketides

DATE-ISSUED: December 10, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ashley; Gary | Alameda | CA | | |
| Chan-Kai; Isaac C. | Hayward | CA | | |
| Burlingame; Mark A. | San Francisco | CA | | |

US-CL-CURRENT: 568/75; 424/70.51

ABSTRACT:

Facile methods for preparing diketide and triketide thioesters are disclosed. The resulting thioesters may be used as intermediates in the synthesis of desired polyketides, and may contain functional groups which ultimately reside in side chains on the resulting polyketide and thus can be used further to manipulate the polyketide so as form derivatives. The polyketides produced may also be tailored by glycosylation, hydroxylation and the like. New polyketides and their derivatives and tailored forms are thereby produced.

17 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 70. Document ID: US 6472371 B1

L2: Entry 70 of 141 File: USPT Oct 29, 2002

US-PAT-NO: 6472371
DOCUMENT-IDENTIFIER: US 6472371 B1

TITLE: Macrolides

DATE-ISSUED: October 29, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Dirlam; John Philip | Gales Ferry | CT | | |
| McArthur; Hamish Alastair Irvine | Mystic | CT | | |
| Blize; Alan Elwood | New London | CT | | |

US-CL-CURRENT: 514/29; 536/124, 536/7.2, 536/7.4

ABSTRACT:

The invention relates to novel erythromycin analogs and azalides, particularly ones with novel C-13 substituents, and to pharmaceutically acceptable salts thereof. The compounds of this invention are antibacterial agents that may be used to treat various bacterial and protozoa infections. The invention also relates to pharmaceutical compositions containing such compounds and to methods of treating bacterial protozoa infections by administering such compounds. The invention also relates to methods of preparing such compounds and to intermediates useful in such preparation.

9 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 71. Document ID: US 6461838 B2

L2: Entry 71 of 141 File: USPT Oct 8, 2002

US-PAT-NO: 6461838
DOCUMENT-IDENTIFIER: US 6461838 B2

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: October 8, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB |
| Ebert-Khosla; Suzanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Fu; Hong | Stanford | CA | | |
| Kao; Camilla | Stanford | CA | | |

US-CL-CURRENT: 435/91.1; 435/183, 435/252.31, 435/252.33, 435/320.1, 536/23.1, 536/23.2

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

12 Claims, 33 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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## 72. Document ID: US 6437151 B2

L2: Entry 72 of 141 File: USPT Aug 20, 2002

US-PAT-NO: 6437151
DOCUMENT-IDENTIFIER: US 6437151 B2

TITLE: Erythromycins and process for their preparation

DATE-ISSUED: August 20, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Leadlay; Peter Francis | Cambridge | | | GB |
| Staunton; James | Cambridge | | | GB |
| Cortes; Jesus | Cambridge | | | GB |
| Pacey; Michael Stephen | Broadstairs | | | GB |

US-CL-CURRENT: 549/271; 536/7.2, 549/13, 549/266, 549/29

ABSTRACT:

Erythromycins, particularly ones with novel C-13 substituents R1 (e.g. C.sub.3 -C.sub.6 cycloalkyl or cycloalkenyl groups) are prepared by fermenting suitable organisms in the presence of R.sub.1 CO.sub.2 H. A preferred organism is Saccharopolyspora erythraea preferably containing an integrated plasmid capable of directing synthesis of desired compounds.

10 Claims, 16 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 73. Document ID: US 6410301 B1

L2: Entry 73 of 141 File: USPT Jun 25, 2002

US-PAT-NO: 6410301
DOCUMENT-IDENTIFIER: US 6410301 B1

TITLE: Myxococcus host cells for the production of epothilones

DATE-ISSUED: June 25, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Julien; Bryan | Oakland | CA | | |
| Katz; Leonard | Hayward | CA | | |
| Khosla; Chaitan | Palo Alto | CA | | |

US-CL-CURRENT: 435/252.3

ABSTRACT:

Recombinant Myxococcus host cell containing recombinant expression vectors containing epothilone polyketide synthase genes can produce epothilones C and D.

6 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 74. Document ID: US 6399382 B1

L2: Entry 74 of 141 File: USPT Jun 4, 2002

US-PAT-NO: 6399382
DOCUMENT-IDENTIFIER: US 6399382 B1
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: June 4, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB |
| Ebert-Khosla; Susanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Kao; Camilla | Stanford | CA | | |

US-CL-CURRENT: 435/440; 435/183, 435/189, 435/232, 435/252.3, 435/252.35, 435/320.1,

435/471, 435/486

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

15 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 75. Document ID: US 6391640 B1

L2: Entry 75 of 141 File: USPT May 21, 2002

US-PAT-NO: 6391640
DOCUMENT-IDENTIFIER: US 6391640 B1

TITLE: Methods and compositions for cellular and metabolic engineering

DATE-ISSUED: May 21, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Minshull; Jeremy | San Francisco | CA | | |
| Stemmer; Willem P. C. | Los Gatos | CA | | |

US-CL-CURRENT: 435/440; 435/6, 435/91.2, 536/23.1, 536/24.3

ABSTRACT:

The present invention is generally directed to the evolution of new metabolic pathways and the enhancement of bioprocessing through a process herein termed recursive sequence recombination. Recursive sequence recombination entails performing iterative cycles of recombination and screening or selection to "evolve" individual genes, whole plasmids or viruses, multigene clusters, or even whole genomes. Such techniques do not require the extensive analysis and computation required by conventional methods for metabolic engineering.

225 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 76. Document ID: US 6391594 B1

L2: Entry 76 of 141 File: USPT May 21, 2002

US-PAT-NO: 6391594
DOCUMENT-IDENTIFIER: US 6391594 B1

TITLE: Modified modular PKS with retained scaffold

DATE-ISSUED: May 21, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Ashley; Gary | Alameda | CA | | |
| Fu; Hong | Stanford | CA | | |
| Kao; Camilla M. | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |

US-CL-CURRENT: 435/91.4; 435/183, 435/193, 435/252.35, 435/320.1, 435/455, 435/471, 435/486, 536/23.2

ABSTRACT:

Combinatorial libraries of polyketides can be obtained by suitable manipulation of a host modular polyketide synthase gene cluster such as that which encodes the PKS for erythromycin. The combinatorial library is useful as a source of pharmaceutically active compounds.

16 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 77. Document ID: US 6388099 B2

L2: Entry 77 of 141 File: USPT May 14, 2002

US-PAT-NO: 6388099
DOCUMENT-IDENTIFIER: US 6388099 B2

TITLE: Production of 8,8a-dihydroxy-6-deoxyerythronolide B

DATE-ISSUED: May 14, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| McDaniel; Robert | Palo Alto | CA | | |

US-CL-CURRENT: 549/264

ABSTRACT:

The heterologous expression of the OlePKS in Streptomyces lividans, produces 8,8a-deoxyoleandolide, an aglycone precursor of oleandomycin. The co-expression with DEBS in S. lividans of the P450 monooxygenase OleP produces 8,8a-dihydroxy-6-deoxyerythonolide B and other derivatives that are precursors to important macrolide antibiotics.

15 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 78. Document ID: US 6383787 B1

L2: Entry 78 of 141 File: USPT May 7, 2002

US-PAT-NO: 6383787
DOCUMENT-IDENTIFIER: US 6383787 B1
**** See image for Certificate of Correction ****

TITLE: Genes for the biosynthesis of epothilones

DATE-ISSUED: May 7, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schupp; Thomas | Mohlin | | | CH |
| Ligon; James Madison | Apex | NC | | |
| Molnar; Istvan | Durham | NC | | |
| Zirkle; Ross | Raleigh | NC | | |
| Cyr; Devon Dawn | Fuquay-Varina | NC | | |
| Gorlach; Jorn | Durham | NC | | |

US-CL-CURRENT: 435/183; 435/193, 435/252.3, 435/252.35, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Nucleic acid molecules are isolated from Sorangium cellulosum that encode polypeptides necessary for the biosynthesis of epothilone. Disclosed are methods for the production of epothilone in recombinant hosts transformed with the genes of the invention. In this manner, epothilone can be produced in quantities large enough to enable their purification and use in pharmaceutical formulations such as those for the treatment of cancer.

25 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 79. Document ID: US 6358719 B1

L2: Entry 79 of 141 File: USPT Mar 19, 2002

US-PAT-NO: 6358719
DOCUMENT-IDENTIFIER: US 6358719 B1

TITLE: Genes for the biosynthesis of epothilones

DATE-ISSUED: March 19, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schupp; Thomas | Mohlin | | | CH |
| Ligon; James Madison | Apex | NC | | |
| Molnar; Istvan | Durham | NC | | |
| Zirkle; Ross | Raleigh | NC | | |
| Cyr; Devon Dawn | Fuquay-Varina | NC | | |
| Gorlach; Jorn | Durham | NC | | |

US-CL-CURRENT: 435/189; 435/252.3, 435/252.35, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Nucleic acid molecules are isolated from Sorangium cellulosum that encode polypeptides necessary for the biosynthesis of epothilone. Disclosed are methods for the production of epothilone in recombinant hosts transformed with the genes of the invention. In this manner, epothilone can be produced in quantities large enough to enable their purification and use in pharmaceutical formulations such as those for the treatment of cancer.

25 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 80. Document ID: US 6358712 B1

L2: Entry 80 of 141 File: USPT Mar 19, 2002

US-PAT-NO: 6358712
DOCUMENT-IDENTIFIER: US 6358712 B1

TITLE: Ordered gene assembly

DATE-ISSUED: March 19, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Jarrell; Kevin A. | Lincoln | MA | | |
| Coljee; Vincent W. | Cambridge | MA | | |
| Donahue; William | Quincy | MA | | |
| Mikheeva; Svetlana | Allston | MA | | |

US-CL-CURRENT: 435/91.1; 435/6, 435/91.2, 435/91.3, 435/91.52, 536/23.1

ABSTRACT:

The present invention provides an improved system for linking nucleic acids to one another. In particular, the present invention provides techniques for producing DNA product molecules that may be easily and directly ligated to recipient molecules. The product molecules need not be cleaved with restriction enzymes in order to undergo such ligation. In preferred embodiments of the invention, the DNA product molecules are produced through iterative DNA synthesis reactions, so that the product molecules are amplified products. The invention further provides methods for directed ligation of product molecules (i.e., for selective ligation of certain molecules within a collection of molecules), and also for methods of exon shuffling, in which multiple different product molecules are produced in a single ligation reaction. Preferred embodiments of the invention involve ligation of product molecules encoding functional protein domains, particularly domains naturally found in conserved gene families. The

inventive DNA manipulation system is readily integrated with other nucleic acid manipulation systems, such as ribozyme-mediated systems, and also is susceptible to automation.

29 Claims, 48 Drawing figures
Exemplary Claim Number: 1,2
Number of Drawing Sheets: 46



| Terms | Documents |
|---|---|
| l1 and (nucleic acid or gene or dna or cdna) | 141 |

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**Search Results** - Record(s) 81 through 100 of 141 returned.

☐ 81. Document ID: US 6355459 B1

L2: Entry 81 of 141 File: USPT Mar 12, 2002

US-PAT-NO: 6355459
DOCUMENT-IDENTIFIER: US 6355459 B1

TITLE: Genes for the biosynthesis of epothilones

DATE-ISSUED: March 12, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schupp; Thomas | Mohlin | | | CH |
| Ligon; James Madison | Apex | NC | | |
| Molnar; Istvan | Durham | NC | | |
| Zirkle; Ross | Raleigh | NC | | |
| Cyr; Devon Dawn | Fuquay-Varina | NC | | |
| Gorlach; Jorn | Durham | NC | | |

US-CL-CURRENT: 435/183; 435/189, 435/193, 435/232, 435/252.3, 435/252.35, 435/320.1, 536/23.2

ABSTRACT:

Nucleic acid molecules are isolated from Sorangium cellulosum that encode polypeptides necessary for the biosynthesis of epothilone. Disclosed are methods for the production of epothilone in recombinant hosts transformed with the genes of the invention. In this manner, epothilone can be produced in quantities large enough to enable their purification and use in pharmaceutical formulations such as those for the treatment of cancer.

115 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 82. Document ID: US 6355458 B1

L2: Entry 82 of 141 File: USPT Mar 12, 2002

US-PAT-NO: 6355458
DOCUMENT-IDENTIFIER: US 6355458 B1

TITLE: Genes for the biosynthesis of epothilones

DATE-ISSUED: March 12, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schupp; Thomas | Mohlin | | | CH |
| Ligon; James Madison | Apex | NC | | |
| Molnar; Istvan | Durham | NC | | |
| Zirkle; Ross | Raleigh | NC | | |
| Cyr; Devon Dawn | Fuquay-Varina | NC | | |
| Gorlach; Jorn | Durham | NC | | |

US-CL-CURRENT: 435/183; 435/189, 435/193, 435/232, 435/252.3, 435/252.35, 435/320.1, 530/300, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Nucleic acid molecules are isolated from Sorangium cellulosum that encode polypeptides necessary for the biosynthesis of epothilone. Disclosed are methods for the production of epothilone in recombinant hosts transformed with the genes of the invention. In this manner, epothilone can be produced in quantities large enough to enable their purification and use in pharmaceutical formulations such as those for the treatment of cancer.

100 Claims, 0 Drawing figures
Exemplary Claim Number: 1



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☐ 83. Document ID: US 6355457 B1

L2: Entry 83 of 141 File: USPT Mar 12, 2002

US-PAT-NO: 6355457
DOCUMENT-IDENTIFIER: US 6355457 B1

TITLE: Genes for the biosynthesis of epothilones

DATE-ISSUED: March 12, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schupp; Thomas | Mohlin | | | CH |
| Ligon; James Madison | Apex | NC | | |
| Molnar; Istvan | Durham | NC | | |
| Zirkle; Ross | Raleigh | NC | | |
| Cyr; Devon Dawn | Fuquay-Varina | NC | | |
| Gorlach; Jorn | Durham | NC | | |

US-CL-CURRENT: 435/183; 435/189, 435/193, 435/195, 435/196, 435/232, 435/252.3, 435/252.35, 435/320.1, 530/300, 536/23.1 , 536/23.2, 536/23.7

ABSTRACT:

Nucleic acid molecules are isolated from Sorangium cellulosum that encode polypeptides necessary for the biosynthesis of epothilone. Disclosed are methods for the production of epothilone in recombinant hosts transformed with the genes of the invention. In this manner, epothilone can be produced in quantities large enough to enable their purification and use in pharmaceutical formulations such as those for the treatment of cancer.

115 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 84. Document ID: US 6346404 B1

L2: Entry 84 of 141 File: USPT Feb 12, 2002

US-PAT-NO: 6346404
DOCUMENT-IDENTIFIER: US 6346404 B1
**** See image for Certificate of Correction ****

TITLE: Genes for the biosynthesis of epothilones

DATE-ISSUED: February 12, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schupp; Thomas | Mohlin | | | CH |
| Ligon; James Madison | Apex | NC | | |
| Molnar; Istvan | Durham | NC | | |
| Zirkle; Ross | Raleigh | NC | | |
| Cyr; Devon Dawn | Fuquay-Varina | NC | | |
| Gorlach; Jorn | Durham | NC | | |

US-CL-CURRENT: 435/183; 435/189, 435/193, 435/232, 435/252.3, 435/252.35, 435/320.1, 530/350, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Nucleic acid molecules are isolated from Sorangium cellulosum that encode polypeptides necessary for the biosynthesis of epothilone. Disclosed are methods for the production of epothilone in recombinant hosts transformed with the genes of the invention. In this manner, epothilone can be produced in quantities large enough to enable their purification and use in pharmaceutical formulations such as those for the treatment of cancer.

85 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 85. Document ID: US 6309883 B1

L2: Entry 85 of 141 File: USPT Oct 30, 2001

US-PAT-NO: 6309883
DOCUMENT-IDENTIFIER: US 6309883 B1
**** See image for Certificate of Correction ****

TITLE: Methods and compositions for cellular and metabolic engineering

DATE-ISSUED: October 30, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Minshull; Jeremy | San Francisco | CA | | |
| Stemmer; Willem P. C. | Los Gatos | CA | | |

US-CL-CURRENT: 435/440; 435/6, 536/23.1, 536/24.3

ABSTRACT:

The present invention is generally directed to the evolution of new metabolic pathways and the enhancement of bioprocessing through a process herein termed recursive sequence recombination. Recursive sequence recombination entails performing iterative cycles of recombination and screening or selection to "evolve" individual genes, whole plasmids or viruses, multigene clusters, or even whole genomes. Such techniques do not require the extensive analysis and computation required by conventional methods for metabolic engineering.

134 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1



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☐ 86. Document ID: US 6303767 B1

L2: Entry 86 of 141 File: USPT Oct 16, 2001

US-PAT-NO: 6303767
DOCUMENT-IDENTIFIER: US 6303767 B1

TITLE: Nucleic acids encoding narbonolide polyketide synthase enzymes from streptomyces narbonensis

DATE-ISSUED: October 16, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Betlach; Melanie C. | San Francisco | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |

US-CL-CURRENT: 536/23.2; 435/320.1, 536/23.1

ABSTRACT:

Host cells comprising recombinant vectors encoding the narbomycin polyketide synthase and narbomycin modification enzymes from Streptomyces narbonensis can be used to produce narbomycin, picromycin, methymycin, and neomethymycin. Recombinant DNA constructs comprising one or more narbomycin polyketide synthase domains, modules, open reading frames, and variants thereof can be used to produce recombinant polyketide synthases and a variety of different polyketides with application in agriculture, medicine, and animal health.

9 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 87. Document ID: US 6303342 B1

L2: Entry 87 of 141 File: USPT Oct 16, 2001

US-PAT-NO: 6303342
DOCUMENT-IDENTIFIER: US 6303342 B1

TITLE: Recombinant methods and materials for producing epothilones C and D

DATE-ISSUED: October 16, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Julien; Bryan | Oakland | CA | | |
| Katz; Leonard | Hayward | CA | | |
| Khosla; Chaitan | Palo Alto | CA | | |
| Tang; Li | Foster City | CA | | |

US-CL-CURRENT: 435/76

ABSTRACT:

Recombinant nucleic acids that encode all or a portion of the epothilone polyketide synthase (PKS) are used to express recombinant PKS genes in host cells for the production of epothilones, epothilone derivatives, and polyketides that are useful as cancer chemotherapeutics, fungicides, and immunosuppressants.

29 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 88. Document ID: US 6280999 B1

L2: Entry 88 of 141 File: USPT Aug 28, 2001

US-PAT-NO: 6280999
DOCUMENT-IDENTIFIER: US 6280999 B1

TITLE: Sorangium polyketide synthases and encoding DNA therefor

DATE-ISSUED: August 28, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Gustafsson; Claes | Belmont | CA | | |
| Betlach; Mary C. | San Francisco | CA | | |
| Ashley; Gary | Alameda | CA | | |
| Julien; Bryan | Oakland | CA | | |
| Ziermann; Rainer | San Mateo | CA | | |

US-CL-CURRENT: 435/252.3; 435/183, 435/320.1, 435/325, 536/23.2

ABSTRACT:

Novel Sorangium polyketide synthases, and domains thereof, and polynucleotides encoding therefor. Additionally, chimeric polyketide synthases that include domains, or subsets of domains, patterned on said novel polyketide synthases. Methods to prepare polyketide combinatorial libraries are described, as are recombinant host cells in which polyketides are produced.

8 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 21

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 89. Document ID: US 6274560 B1

L2: Entry 89 of 141 File: USPT Aug 14, 2001

US-PAT-NO: 6274560
DOCUMENT-IDENTIFIER: US 6274560 B1

TITLE: Cell-free synthesis of polyketides

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Pieper; Rembert | Washington | DC | | |
| Luo; Guanglin | Madison | CT | | |
| Cane; David E. | Providence | RI | | |
| Kao; Camilla | Palo Alto | CA | | |

US-CL-CURRENT: 514/29; 435/252.3, 435/252.35, 435/320.1, 435/471

ABSTRACT:

Cell-free systems which effect the production of polyketides employing modular polyketide synthases are described. Libraries of new and/or known polyketides may also be produced in cell-free systems employing aromatic PKS, modular PKS or both.

13 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 90. Document ID: US 6274350 B1

L2: Entry 90 of 141 File: USPT Aug 14, 2001

US-PAT-NO: 6274350
DOCUMENT-IDENTIFIER: US 6274350 B1
**** See image for Certificate of Correction ****

TITLE: Biosynthetic genes for spinosyn insecticide production

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Baltz; Richard H. | Indianapolis | IN | | |
| Crawford; Kathryn P. | Indianapolis | IN | | |
| Broughton; M. Christine | Indianapolis | IN | | |
| Madduri; Krishnamurthy | Woodlawn | OH | | |
| Merlo; Donald J. | Carmel | IN | | |
| Turner; Jan R. | Carmel | IN | | |
| Treadway; Patti J. | Greenwood | IN | | |
| Waldron; Clive | Indianapolis | IN | | |

US-CL-CURRENT: 435/76; 435/254.2, 435/320.1, 536/23.2

ABSTRACT:

Spinosyn biosynthetic genes, spinosyn producing microorganisms transformed with the biosynthetic genes, methods using the biosynthetic genes to increase production of spinosyn insecticidal macrolides, and methods using the genes or fragments thereof to change the products produced by spinosyn-producing microorganisms.

9 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6



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☐ 91. Document ID: US 6271255 B1

L2: Entry 91 of 141 File: USPT Aug 7, 2001

US-PAT-NO: 6271255
DOCUMENT-IDENTIFIER: US 6271255 B1

TITLE: Erythromycins and process for their preparation

DATE-ISSUED: August 7, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Leadlay; Peter Francis | Cambridge | | | GB |
| Staunton; James | Cambridge | | | GB |
| Cortes; Jesus | Cambridge | | | GB |
| Pacey; Michael Stephen | Broadstairs | | | GB |

US-CL-CURRENT: 514/450; 514/29, 536/7.2, 549/13, 549/266, 549/271, 549/29

ABSTRACT:

Erythromycins, particularly with C-13 substituents R1 (e.g. C.sub.3 -C.sub.6 cycloalkyl

or cycloalkenyl groups) are prepared by fermenting suitable organisms in the presence of R.sub.1 CO.sub.2 H. A preferred organism is Saccharopolyspora erythraea preferably containing an integrated plasmid capable of directing synthesis of desired compounds.

27 Claims, 16 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 92. Document ID: US 6265202 B1

L2: Entry 92 of 141 File: USPT Jul 24, 2001

US-PAT-NO: 6265202
DOCUMENT-IDENTIFIER: US 6265202 B1

TITLE: DNA encoding methymycin and pikromycin

DATE-ISSUED: July 24, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Sherman; David H. | St. Louis Park | MN | | |
| Liu; Hung-Wen | Roseville | MN | | |
| Xue; Yongquan | St. Paul | MN | | |
| Zhao; Lishan | St. Paul | MN | | |

US-CL-CURRENT: 435/252.31; 435/183, 435/252.3, 435/252.33, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

A novel pathway for the synthesis of polyhydroxyalkanoates is provided. A method of synthesizing a recombinant polyhydroxyalkanoate monomer synthase is also provided. These recombinant polyhydroxyalkanoate synthases are derived from multifunctional fatty acid synthases or polyketide synthases and generate hydroxyacyl acids capable of polymerization by a polyhydroxyalkanoate synthase. Also provided is a biosynthetic gene cluster for methymycin and pikomycin as well as a biosynthetic gene cluster for desosamine.

8 Claims, 160 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 158

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 93. Document ID: US 6262340 B1

L2: Entry 93 of 141 File: USPT Jul 17, 2001

US-PAT-NO: 6262340
DOCUMENT-IDENTIFIER: US 6262340 B1

TITLE: Production of polyketides in plants

DATE-ISSUED: July 17, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Betlach; Mary C. | San Francisco | CA | | |
| Kealey; James T. | Davis | CA | | |
| Gutterson; Neal | Oakland | CA | | |
| Ralston; Ed | Pleasant Hill | CA | | |

US-CL-CURRENT: 800/278; 435/410, 435/411, 435/419, 435/69.1, 800/281, 800/284

ABSTRACT:

The present invention provides genetically altered plants and plant cells that have been modified to contain expression system(s) capable of expressing a functional polyketide synthase (PKS). The present invention further provides methods of producing PKS and polyketides using these plants and cells.

65 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3



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☐ 94. Document ID: US 6261842 B1

L2: Entry 94 of 141 File: USPT Jul 17, 2001

US-PAT-NO: 6261842
DOCUMENT-IDENTIFIER: US 6261842 B1
**** See image for Certificate of Correction ****

TITLE: Microorganism genomics, compositions and methods related thereto

DATE-ISSUED: July 17, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Handelsman; Jo | Madison | WI | | |
| Goodman; Robert M. | Madison | WI | | |
| Rondon; Michelle R. | Madison | WI | | |

US-CL-CURRENT: 435/479; 435/252.3, 536/23.1

ABSTRACT:

The present invention provides methods and compositions for accessing, in a generally unbaised manner, a diverse genetic pool for genes involved in biosynthetic pathways. The invention also provides compounds which can be identified by cloning biosynthetic pathways.

32 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 95. Document ID: US 6261816 B1

L2: Entry 95 of 141 File: USPT Jul 17, 2001

US-PAT-NO: 6261816
DOCUMENT-IDENTIFIER: US 6261816 B1

TITLE: Method to produce novel polyketides

DATE-ISSUED: July 17, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Pieper; Rembert | Washington | DC | | |
| Luo; Guanglin | Madison | CT | | |
| Cane; David E. | Providence | RI | | |
| Kao; Camilla | Palo Alto | CA | | |

US-CL-CURRENT: 435/183; 435/91.1, 435/91.4, 435/91.41, 435/91.42, 536/23.2

ABSTRACT:

Modified PKS gene clusters which produce novel polyketides in an efficient system in a host cell or in a cell free extract are described.

10 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 96. Document ID: US 6258566 B1

L2: Entry 96 of 141 File: USPT Jul 10, 2001

US-PAT-NO: 6258566
DOCUMENT-IDENTIFIER: US 6258566 B1
**** See image for Certificate of Correction ****

TITLE: Production of polyketides in bacteria and yeast

DATE-ISSUED: July 10, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Barr; Philip J. | Oakland | CA | | |
| Santi; Daniel V. | San Francisco | CA | | |
| Ashley; Gary W. | Alameda | CA | | |
| Ziermann; Rainer | San Mateo | CA | | |

US-CL-CURRENT: 435/76; 435/183, 435/252.3, 435/252.33, 435/252.6, 435/254.11, 435/254.2, 435/320.1, 435/325, 435/419

ABSTRACT:

Hybrid and novel polyketide synthases (PKSs) and polyketides are produced by use of a multiple vector system. The combinatorial possibilities offered by placing the various catalytic activities of PKS systems on separate vectors permits the construction of improved libraries of PKS and polyketides. In addition, polyketides can be produced in hosts that ordinarily do not produce polyketides by supplying, along with an expression system for the desired PKS, an expression system for holo acyl carrier protein (ACP) synthase.

17 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 97. Document ID: US 6251636 B1

L2: Entry 97 of 141 File: USPT Jun 26, 2001

US-PAT-NO: 6251636
DOCUMENT-IDENTIFIER: US 6251636 B1

TITLE: Recombinant oleandolide polyketide synthase

DATE-ISSUED: June 26, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Betlach; Mary C. | San Francisco | CA | | |
| Shah; Sanjay Krishnakant | Concord | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Tang; Li | Foster City | CA | | |

US-CL-CURRENT: 435/76; 435/252.35, 435/254.2, 435/320.1, 435/325, 435/419, 536/23.1, 536/23.2

ABSTRACT:

Recombinant DNA compounds that encode all or a portion of the oleandolide polyketide synthase are used to express recombinant polyketide synthase genes in host cells for the production of oleandolide, oleandolide derivatives, and polyketides that are useful as antibiotics and motilides.

22 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 98. Document ID: US 6248579 B1

L2: Entry 98 of 141 File: USPT Jun 19, 2001

US-PAT-NO: 6248579
DOCUMENT-IDENTIFIER: US 6248579 B1
**** See image for Certificate of Correction ****

TITLE: Streptomyces avermitilis gene directing the ratio of B2:B1 avermectins

DATE-ISSUED: June 19, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Stutzman-Engwall; Kim J. | East Lyme | CT | | |
| McArthur; Hamish | Gales Ferry | CT | | |
| Katoh; Yoshihiro | Aichi | | | JP |

US-CL-CURRENT: 435/253.5; 435/119, 435/471, 435/75, 435/76, 536/23.1, 536/7.1

ABSTRACT:

The present invention relates to polynucleotide molecules comprising nucleotide sequences encoding an aveC gene product, which polynucleotide molecules can be used to alter the ratio or amount of class 2:1 avermectins produced in fermentation cultures of S. avermitilis. The present invention further relates to vectors, host cells, and mutant strains of S. avermitilis in which the aveC gene has been inactivated, or mutated so as to change the ratio or amount of class 2:1 avermectins produced.

14 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7



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☐ 99. Document ID: US 6215007 B1

L2: Entry 99 of 141 File: USPT Apr 10, 2001

US-PAT-NO: 6215007
DOCUMENT-IDENTIFIER: US 6215007 B1
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB |
| Ebert-Khosla; Suzanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Fu; Hong | Stanford | CA | | |

US-CL-CURRENT: 549/417; 549/389, 549/400, 560/128, 562/433, 562/435, 562/461

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known

polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

20 Claims, 32 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 100. Document ID: US 6214573 B1

L2: Entry 100 of 141 File: USPT Apr 10, 2001

US-PAT-NO: 6214573
DOCUMENT-IDENTIFIER: US 6214573 B1

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB |
| Ebert-Khosla; Suzanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Fu; Hong | Stanford | CA | | |

US-CL-CURRENT: 435/41; 435/132, 435/133, 435/147, 435/148, 435/252.3, 435/252.33, 435/252.35

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

21 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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| Terms | Documents |
|---|---|
| l1 and (nucleic acid or gene or dna or cdna) | 141 |

WEST

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**Search Results** - Record(s) 101 through 120 of 141 returned.

☐ 101. Document ID: US 6200813 B1

L2: Entry 101 of 141 File: USPT Mar 13, 2001

US-PAT-NO: 6200813
DOCUMENT-IDENTIFIER: US 6200813 B1
**** See image for Certificate of Correction ****

TITLE: Polyketide derivatives and recombinant methods for making same

DATE-ISSUED: March 13, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Katz; Leonard | Wheeling | IL | | |
| Stassi; Diane L. | Highland Park | IL | | |
| Summers, Jr.; Richard G. | Nashotah | WI | | |
| Ruan; Xiaoan | Lake Bluff | IL | | |
| Pereda-Lopez; Ana | Mundelein | IL | | |
| Kakavas; Stephan J. | Buffalo Grove | IL | | |

US-CL-CURRENT: 435/477; 435/252.3, 435/252.35, 435/320.1, 435/69.1, 435/69.7, 536/23.2, 536/23.4

ABSTRACT:

The invention provides novel erythromycin derivatives in which methyl groups on the macrolactone ring have been substituted with --H, -Et, and/or --OH. The invention also provides reagents such as isolated polynucleotides, vectors comprising the polynucleotides and host cells transformed with the vectors for making the novel compounds. Methods for making the compounds utilizing genetic engineering techniques are also disclosed.

27 Claims, 47 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 47

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 102. Document ID: US 6197591 B1

L2: Entry 102 of 141 File: USPT Mar 6, 2001

US-PAT-NO: 6197591
DOCUMENT-IDENTIFIER: US 6197591 B1

TITLE: Streptomyces avermitilis regulatory genes for increased avermectin production

DATE-ISSUED: March 6, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Stutzman-Engwall; Kim J. | East Lyme | CT | | |
| Price; Brenda S. | Antioch | IL | | |

US-CL-CURRENT: 435/486; 435/183, 435/252.3, 435/253.5, 435/254.11, 435/320.1, 435/325, 435/419, 435/69.1, 435/76

ABSTRACT:

The present invention is directed to compositions and methods for producing avermectins, and is primarily in the field of animal health. The present invention relates to the identification and characterization of two novel genes, herein referred to as the aveR1 and aveR2 genes, that are involved in regulating avermectin polyketide synthase (PKS) expression and avermectin biosynthesis in Streptomyces avermitilis. The present invention is based on the discovery that inactivation of these genes results in an increase in the amount of avermectin produced by S. avermitilis.

36 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 103. Document ID: US 6177262 B1

L2: Entry 103 of 141 File: USPT Jan 23, 2001

US-PAT-NO: 6177262
DOCUMENT-IDENTIFIER: US 6177262 B1

TITLE: Recombinant host cells for the production of polyketides

DATE-ISSUED: January 23, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ziermann; Rainer | San Mateo | CA | | |
| Betlach; Mary C. | San Francisco | CA | | |

US-CL-CURRENT: 435/76; 435/252.35

ABSTRACT:

Yields of polyketides produced in host cells such as Streptomyces can be increased by coexpression of the ptpA gene. The introduction of recombinant vectors encoding ptpA and polyketide synthase genes is more efficient and does not require methyl-free DNA if the host cell is a restriction/methylation deficient strain, such as Streptomyces lividans K4-114, K4-155, or K27-39.

13 Claims, 0 Drawing figures
Exemplary Claim Number: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 104. Document ID: US 6143526 A

L2: Entry 104 of 141 File: USPT Nov 7, 2000

US-PAT-NO: 6143526
DOCUMENT-IDENTIFIER: US 6143526 A
**** See image for Certificate of Correction ****

TITLE: Biosynthetic genes for spinosyn insecticide production

DATE-ISSUED: November 7, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Baltz; Richard H. | Indianapolis | IN | 46220 | |
| Broughton; M. Christine | Indianapolis | IN | 46220 | |
| Crawford; Kathryn P. | Indianapolis | IN | 46201 | |
| Madduri; Krishnamurthy | Woodlawn | OH | 45215 | |
| Merlo; Donald J. | Carmel | IN | 46032 | |
| Treadway; Patti J. | Greenwood | IN | 46143 | |
| Turner; Jan R. | Carmel | IN | 46032 | |
| Waldron; Clive | Indianapolis | IN | 46220 | |

US-CL-CURRENT: 435/76; 435/183, 435/189, 435/254.2, 435/320.1, 536/23.2

ABSTRACT:

Spinosyn biosynthetic genes, spinosyn producing microorganisms transformed with the biosynthetic genes, methods using the biosynthetic genes to increase production of spinosyn insecticidal macrolides, and methods using the genes or fragments thereof to change the products produced by spinosyn-producing microorganisms.

23 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 105. Document ID: US 6121029 A

L2: Entry 105 of 141 File: USPT Sep 19, 2000

US-PAT-NO: 6121029
DOCUMENT-IDENTIFIER: US 6121029 A

TITLE: Genes for the biosynthesis of epothilones

DATE-ISSUED: September 19, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schupp; Thomas | Mohlin | | | CH |
| Ligon; James Madison | Apex | NC | | |
| Molnar; Istvan | Durham | NC | | |
| Zirkle; Ross | Raleigh | NC | | |
| Cyr; Devon Dawn | Fuquay-Varina | NC | | |
| Gorlach; Jorn | Durham | NC | | |

US-CL-CURRENT: 435/183; 435/189, 435/193, 435/232, 435/252.3, 435/252.35, 435/320.1, 530/300, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Nucleic acid molecules are isolated from Sorangium cellulosum that encode polypeptides necessary for the biosynthesis of epothilone. Disclosed are methods for the production of epothilone in recombinant hosts transformed with the genes of the invention. In this manner, epothilone can be produced in quantities large enough to enable their purification and use in pharmaceutical formulations such as those for the treatment of cancer.

115 Claims, 0 Drawing figures
Exemplary Claim Number: 1



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☐ 106. Document ID: US 6117670 A

L2: Entry 106 of 141 File: USPT Sep 12, 2000

US-PAT-NO: 6117670
DOCUMENT-IDENTIFIER: US 6117670 A

TITLE: Pyrrolnitrin biosynthesis genes and uses thereof

DATE-ISSUED: September 12, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James Madison | Apex | NC | | |
| Hill; Dwight Steven | Cary | NC | | |
| Lam; Stephen Ting | Raleigh | NC | | |
| Hammer; Philip Eugene | Cary | NC | | |
| van Pee; Karl-Heinz | Bannewitz | | | DE |
| Kirner; Sabine | Puchheim | | | DE |
| Young; Thomas R. | Vero Beach | FL | | |

US-CL-CURRENT: 435/252.33; 435/189, 435/232, 435/252.3, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

The present invention is directed to the production of pyrrolnitrin in a host via recombinant expression of the polypeptides needed to biologically synthesize pyrrolnitrin. Genes isolated from P. fluorescens, P. pyrrocinia, B. cepacia, and M. fulvus that encode polypeptides necessary to produce pyrrolnitrin are provided, along with methods for identifying and isolating genes needed to recombinantly biosynthesize pyrrolnitrin from any organism capable of producing pyrrolnitrin. The isolated genes

may be transformed and expressed in a desired host organisms to produce pyrrolnitrin according to the invention for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of pyrrolnitrin.

38 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 107. Document ID: US 6117659 A

L2: Entry 107 of 141 File: USPT Sep 12, 2000

US-PAT-NO: 6117659
DOCUMENT-IDENTIFIER: US 6117659 A

TITLE: Recombinant narbonolide polyketide synthase

DATE-ISSUED: September 12, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ashley; Gary | Alameda | CA | | |
| Betlach; Melanie C. | Burlingame | CA | | |
| Betlach; Mary | San Francisco | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Tang; Li | Foster City | CA | | |

US-CL-CURRENT: 435/155; 435/132, 435/189, 435/252.3, 435/252.33, 435/252.35, 435/320.1, 536/23.2, 536/23.7

ABSTRACT:

Recombinant DNA compounds that encode all or a portion of the narbonolide polyketide synthase are used to express recombinant polyketide synthase genes in host cells for the production of narbonolide, narbonolide derivatives, and polyketides that are useful as antibiotics and as intermediates in the synthesis of compounds with pharmaceutical value.

11 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 108. Document ID: US 6090601 A

L2: Entry 108 of 141 File: USPT Jul 18, 2000

US-PAT-NO: 6090601
DOCUMENT-IDENTIFIER: US 6090601 A

TITLE: Sorangium polyketide synthase

DATE-ISSUED: July 18, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Gustafsson; Claes | Belmont | CA | | |
| Betlach; Mary C. | San Francisco | CA | | |

US-CL-CURRENT: 435/183; 435/252.3, 435/320.1, 435/325, 536/23.2

ABSTRACT:

Domains of epothilone polyketide synthase, and polynucleotides encoding therefor. Additionally, chimeric polyketide synthases that include domains, or subsets of domains, patterned on epothilone polyketide synthase. Methods to prepare epothilone in pharmaceutically useful quantitites are described, as are methods to prepare polyketide combinatorial libraries.

24 Claims, 12 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 109. Document ID: US 6080555 A

L2: Entry 109 of 141 File: USPT Jun 27, 2000

US-PAT-NO: 6080555
DOCUMENT-IDENTIFIER: US 6080555 A

TITLE: Synthesis of polyketides from diketides

DATE-ISSUED: June 27, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Pieper; Rembert | Washington | DC | | |
| Luo; Guanglin | Providence | RI | | |
| Cane; David E. | Providence | RI | | |

US-CL-CURRENT: 435/41; 435/64, 435/7.1

ABSTRACT:

Cell-free systems which effect the production of polyketides employing modular polyketide synthases are described. Libraries of new and/or known polyketides may also be produced in cell-free systems employing aromatic PKS, modular PKS or both.

14 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 110. Document ID: US 6077696 A

L2: Entry 110 of 141 File: USPT Jun 20, 2000

US-PAT-NO: 6077696
DOCUMENT-IDENTIFIER: US 6077696 A

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: June 20, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB |
| Ebert-Khosla; Suzanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Fu; Hong | Stanford | CA | | |
| Kao; Camilla | Stanford | CA | | |

US-CL-CURRENT: 435/135; 435/132, 435/147, 435/148, 435/183, 435/252.3, 435/252.33, 435/252.35, 435/320.1, 536/23.1, 536/23.2

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

6 Claims, 33 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 111. Document ID: US 6066721 A

L2: Entry 111 of 141 File: USPT May 23, 2000

US-PAT-NO: 6066721
DOCUMENT-IDENTIFIER: US 6066721 A
**** See image for Certificate of Correction ****

TITLE: Method to produce novel polyketides

DATE-ISSUED: May 23, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CT | | |
| Pieper; Rembert | Menlo Park | CA | | |
| Luo; Guanglin | Providence | RI | | |
| Cane; David E. | Providence | RI | | |
| Kao; Camilla | Palo Alto | CA | | |

US-CL-CURRENT: 536/23.1; 435/252.3, 435/252.35, 435/320.1, 435/7.1, 536/23.2

ABSTRACT:

Modified PKS gene clusters which produce novel polyketides in an efficient system in a host cell or in a cell free extract are described.

12 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 112. Document ID: US 6063561 A

L2: Entry 112 of 141 File: USPT May 16, 2000

US-PAT-NO: 6063561
DOCUMENT-IDENTIFIER: US 6063561 A

TITLE: Polyketide derivatives and recombinant methods for making same

DATE-ISSUED: May 16, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Katz; Leonard | Wheeling | IL | | |
| Stassi; Diane L. | Highland Park | IL | | |
| Summers, Jr.; Richard G. | Appleton | WI | | |
| Ruan; Xiaoan | Lake Bluff | IL | | |
| Pereda-Lopez; Ana | Mundelein | IL | | |
| Kakavas; Stephan J. | Buffalo Grove | IL | | |

US-CL-CURRENT: 435/4; 435/15, 435/29, 514/29, 536/7.2

ABSTRACT:

The invention provides novel erythromycin derivatives in which methyl groups on the macrolactone ring have been substituted with --H, -Et, and/or --OH and the ethyl side-chain has been substituted with hydroxymethyl or dihydroxycyclohexylmethyl side-chains. The invention also provides reagents such as isolated polynucleotides, vectors comprising the polynucleotides and host cells transformed with the vectors for making the novel compounds. Methods for making the compounds utilizing genetic engineering techniques are also disclosed.

22 Claims, 32 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 36

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 113. Document ID: US 6060234 A

L2: Entry 113 of 141 File: USPT May 9, 2000

US-PAT-NO: 6060234
DOCUMENT-IDENTIFIER: US 6060234 A

TITLE: Polyketide derivatives and recombinant methods for making same

DATE-ISSUED: May 9, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Katz; Leonard | Wheeling | IL | | |
| Stassi; Diane L. | Highland Park | IL | | |
| Summers, Jr.; Richard G. | Nashotah | WI | | |
| Ruan; Xiaoan | Lake Bluff | IL | | |
| Pereda-Lopez; Ana | Mundelein | IL | | |
| Kakavas; Stephan J. | Buffalo Grove | IL | | |

US-CL-CURRENT: 435/4; 435/32, 514/29, 536/7.2

ABSTRACT:

The invention provides novel erythromycin derivatives in which methyl groups on the macrolactone ring have been substituted with --H, --Et, and/or --OH. The invention also provides reagents such as isolated polynucleotides, vectors comprising the polynucleotides and host cells transformed with the vectors for making the novel compounds. Methods for making the compounds utilizing genetic engineering techniques are also disclosed.

29 Claims, 44 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 47



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☐ 114. Document ID: US 6033883 A

L2: Entry 114 of 141 File: USPT Mar 7, 2000

US-PAT-NO: 6033883
DOCUMENT-IDENTIFIER: US 6033883 A
**** See image for Certificate of Correction ****

TITLE: Production of polyketides in bacteria and yeast

DATE-ISSUED: March 7, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Barr; Philip J. | Oakland | CA | | |
| Santi; Daniel V. | San Francisco | CA | | |
| Ashley; Gary W. | Alameda | CA | | |
| Ziermann; Rainer | San Mateo | CA | | |

US-CL-CURRENT: 435/148; 435/252.33, 435/254.21, 435/320.1, 435/471, 435/477, 435/483, 435/484, 435/486, 435/488, 435/69.1, 435/69.7, 536/23.2, 536/23.4, 536/23.7

ABSTRACT:

Hybrid and novel polyketide synthases and polyketides are produced by use of a multiple vector system. The combinatorial possibilities offered by placing the various catalytic activities of PKS systems on separate vectors permits the construction of improved libraries of PKS and polyketides. In addition, polyketides can be produced in hosts that ordinarily do not produce polyketides by supplying, along with an expression system for the desired PKS, an expression system for holo ACP synthase.

58 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 115. Document ID: US 6022731 A

L2: Entry 115 of 141 File: USPT Feb 8, 2000

US-PAT-NO: 6022731
DOCUMENT-IDENTIFIER: US 6022731 A

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: February 8, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB |
| Ebert-Khosla; Suzanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |

US-CL-CURRENT: 435/252.35; 435/252.3, 435/252.33, 435/320.1, 435/471, 435/476, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

45 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 116. Document ID: US 6004787 A

L2: Entry 116 of 141 File: USPT Dec 21, 1999

US-PAT-NO: 6004787
DOCUMENT-IDENTIFIER: US 6004787 A

TITLE: Method of directing biosynthesis of specific polyketides

DATE-ISSUED: December 21, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Katz; Leonard | Waukegan | IL | | |
| Donadio; Stefano | Libertyville | IL | | |
| McAlpine; James B. | Libertyville | IL | | |

US-CL-CURRENT: 435/183; 435/252.3, 435/252.35, 435/320.1, 435/471, 536/23.2

ABSTRACT:

A method to produce novel polyketide structures by designing and introducing specified changes in the DNA governing the synthesis of the polyketide is disclosed. The biosynthesis of specific polyketide analogs is accomplished by genetic manipulation of a polyketide-producing microorganism by isolating a polyketide biosynthetic gene-containing DNA sequence, identifying enzymatic activities associated within the DNA sequence, introducing one or more specified changes into the DNA sequence which codes for one of the enzymatic activities which results in an altered DNA sequence, introducing the altered DNA sequence into the polyketide-producing microorganism to replace the original sequence, growing a culture of the altered microorganism under conditions suitable for the formation of the specific polyketide analog, and isolating the specific polyketide analog from the culture. The method is most useful when the segment of the chromosome modified is involved in an enzymatic activity associated with polyketide biosynthesis, particularly for manipulating polyketide synthase genes from Saccarharopolyspora or Streptomyces.

39 Claims, 96 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 93

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 117. Document ID: US 5998194 A

L2: Entry 117 of 141 File: USPT Dec 7, 1999

US-PAT-NO: 5998194
DOCUMENT-IDENTIFIER: US 5998194 A

TITLE: Polyketide-associated sugar biosynthesis genes

DATE-ISSUED: December 7, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Summers, Jr.; Richard G. | Nashotah | WI | | |
| Katz; Leonard | Wheeling | IL | | |
| Donadio; Stefano | Varese | | | IT |
| Staver; Michael J. | Grayslake | IL | | |

US-CL-CURRENT: 435/252.33; 435/200, 435/227, 435/228, 435/231, 435/252.3, 435/252.35, 435/320.1, 435/325, 435/419, 536/23.2

ABSTRACT:

The present invention provides isolated polynucleotides from Saccharomyces erythraea

that encode enzymes involved in the biosynthesis of polyketide-associated sugars. Methods of using the polynucleotides to produce novel glycosylation modified polyketides are also provided.

19 Claims, 35 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 45

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 118. Document ID: US 5976830 A

L2: Entry 118 of 141 File: USPT Nov 2, 1999

US-PAT-NO: 5976830
DOCUMENT-IDENTIFIER: US 5976830 A
**** See image for Certificate of Correction ****

TITLE: Methods of producing doxorubicin

DATE-ISSUED: November 2, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Strohl; William R. | Dublin | OH | | |
| Dickens; Michael L. | Columbus | OH | | |
| Desanti; Charles L. | Columbus | OH | | |

US-CL-CURRENT: 435/41; 435/189, 435/252.3, 435/252.33, 435/252.35, 435/320.1, 435/78, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

The present invention provides novel methods for producing doxorubicin using daunomycin as a substrate. One method employs a genetically engineered host microorganism which is transformed with a vector, preferably a plasmid, which contains the doxA gene. Preferably, the doxA gene, also referred to herein as "doxA", is cloned into a plasmid which is then introduced into the host microorganism, preferably a bacterial host, more preferably Streptomyces, to provide a transformed host microorganism. The doxA gene, when present on a plasmid, confers on the transformed host the ability to convert daunomycin and 13-dihydrodaunomycin, to doxorubicin. The doxA gene encodes a P450-like enzyme which catalyzes the hydroxylation of daunomycin and 13-dihydrodaunomycin at C-14 to form doxorubicin; such enzyme is designated "daunomycin C-14 hydroxylase". Thus, the expression of doxA in the transformed host using a plasmid which contains doxA enables the transformed host to convert daunomycin to doxorubicin. The doxorubicin is then extracted from host microorganism cultures.

17 Claims, 21 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 21

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 119. Document ID: US 5962293 A

L2: Entry 119 of 141 File: USPT Oct 5, 1999

US-PAT-NO: 5962293
DOCUMENT-IDENTIFIER: US 5962293 A

TITLE: Methods of producing doxorubicin

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Strohl; William R. | Dublin | OH | | |
| Dickens; Michael L. | Columbus | OH | | |
| Desanti; Charles L. | Columbus | OH | | |

US-CL-CURRENT: 435/189; 435/183, 435/252.3, 435/252.33, 435/320.1, 536/23.2

ABSTRACT:

The present invention provides novel methods for producing doxorubicin using daunomycin as a substrate. One method employs a genetically engineered host microorganism which is transformed with a vector, preferably a plasmid, which contains the doxA gene. Preferably, the doxA gene, also referred to herein as "doxA", is cloned into a plasmid which is then introduced into the host microorganism, preferably a bacterial host, more preferably Streptomyces, to provide a transformed host microorganism. The doxA gene, when present on a plasmid, confers on the transformed host the ability to convert daunomycin and 13-dihydrodaunomycin, to doxorubicin. The doxA gene encodes a P450-like enzyme which catalyzes the hydroxylation of daunomycin and 13-dihydrodaunomycin at C-14 to form doxorubicin; such enzyme is designated "daunomycin C-14 hydroxylase". Thus, the expression of doxA in the transformed host using a plasmid which contains doxA enables the transformed host to convert daunomycin to doxorubicin. The doxorubicin is then extracted from host microorganism cultures.

4 Claims, 12 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 21



☐ 120. Document ID: US 5962290 A

L2: Entry 120 of 141 File: USPT Oct 5, 1999

US-PAT-NO: 5962290
DOCUMENT-IDENTIFIER: US 5962290 A

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB |
| Ebert-Khosla; Suzanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Fu; Hong | Stanford | CA | | |
| Kao; Camilla | Stanford | CA | | |

US-CL-CURRENT: 435/183; 435/252.3, 435/252.33, 435/252.35, 435/320.1, 435/471, 435/476, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

21 Claims, 33 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

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**Search Results** - Record(s) 121 through 140 of 141 returned.

☐ 121. Document ID: US 5945320 A

L2: Entry 121 of 141 File: USPT Aug 31, 1999

US-PAT-NO: 5945320
DOCUMENT-IDENTIFIER: US 5945320 A

TITLE: Platenolide synthase gene

DATE-ISSUED: August 31, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Burgett; Stanley G. | Indianapolis | IN | | |
| Kuhstoss; Stuart A. | Indianapolis | IN | | |
| Rao; Ramachandra N. | Indianapolis | IN | | |
| Richardson; Mark A. | Bloomington | IN | | |
| Rosteck, Jr.; Paul R. | Indianapolis | IN | | |

US-CL-CURRENT: 435/183; 435/252.3, 435/252.35, 435/320.1, 435/69.1, 530/350, 536/23.2

ABSTRACT:

A DNA molecule isolated from Streptomyces ambofaciens encodes the multi-functional proteins which direct the synthesis of the polyketide platenolide.

25 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 122. Document ID: US 5876991 A

L2: Entry 122 of 141 File: USPT Mar 2, 1999

US-PAT-NO: 5876991
DOCUMENT-IDENTIFIER: US 5876991 A

TITLE: Polyketide synthase genes

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| DeHoff; Bradley S. | Indianapolis | IN | | |
| Kuhstoss; Stuart A. | Indianapolis | IN | | |
| Rosteck, Jr.; Paul R. | Indianapolis | IN | | |
| Sutton; Kimberly L. | New Palestine | IN | | |

US-CL-CURRENT: 435/183; 435/252.35, 435/320.1, 435/471, 435/486, 435/69.7, 536/23.2, 536/23.4

ABSTRACT:

A DNA molecule isolated from Streptomyces fradiae encodes the multi-functional proteins which direct the synthesis of the polyketide tylactone.

23 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 123. Document ID: US 5843718 A

L2: Entry 123 of 141 File: USPT Dec 1, 1998

US-PAT-NO: 5843718
DOCUMENT-IDENTIFIER: US 5843718 A
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB2 |
| Ebert-Khosla; Susanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Fu; Hong | Stanford | CA | | |

US-CL-CURRENT: 435/69.1; 435/183, 435/252.3, 435/325

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

21 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

☐ 124. Document ID: US 5837458 A

L2: Entry 124 of 141 File: USPT Nov 17, 1998

US-PAT-NO: 5837458
DOCUMENT-IDENTIFIER: US 5837458 A
**** See image for Certificate of Correction ****

TITLE: Methods and compositions for cellular and metabolic engineering

DATE-ISSUED: November 17, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Minshull; Jeremy | San Francisco | CA | | |
| Stemmer; Willem P. C. | Los Gatos | CA | | |

US-CL-CURRENT: 435/6

ABSTRACT:

The present invention is generally directed to the evolution of new metabolic pathways and the enhancement of bioprocessing through a process herein termed recursive sequence recombination. Recursive sequence recombination entails performing iterative cycles of recombination and screening or selection to "evolve" individual genes, whole plasmids or viruses, multigene clusters, or even whole genomes. Such techniques do not require the extensive analysis and computation required by conventional methods for metabolic engineering.

36 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 125. Document ID: US 5830750 A

L2: Entry 125 of 141 File: USPT Nov 3, 1998

US-PAT-NO: 5830750
DOCUMENT-IDENTIFIER: US 5830750 A
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB2 |
| Ebert-Khosla; Suzanne | Stanford | CA | | |

US-CL-CURRENT: 435/252.35; 435/252.3, 435/254.11, 435/325

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

8 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 126. Document ID: US 5824513 A

L2: Entry 126 of 141 File: USPT Oct 20, 1998

US-PAT-NO: 5824513
DOCUMENT-IDENTIFIER: US 5824513 A

TITLE: Recombinant DNA method for producing erythromycin analogs

DATE-ISSUED: October 20, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Katz; Leonard | Waukegan | IL | | |
| Donadio; Stefano | Libertyville | IL | | |
| McAlpine; James B. | Libertyville | IL | | |

US-CL-CURRENT: 435/76; 435/252.35, 435/320.1, 435/69.1, 514/29, 536/23.2

ABSTRACT:

A method to produce novel polyketide structures by designing and introducing specified changes in the DNA governing the synthesis of the polyketide is disclosed. The biosynthesis of specific polyketide analogs is accomplished by genetic manipulation of a polyketide-producing microorganism by isolating a polyketide biosynthetic gene-containing DNA sequence, identifying enzymatic activities associated within the DNA sequence, introducing one or more specified changes into the DNA sequence which codes for one of the enzymatic activities which results in an altered DNA sequence, introducing the altered DNA sequence into the polyketide-producing microorganism to replace the original sequence, growing a culture of the altered microorganism under conditions suitable for the formation of the specific polyketide analog, and isolating the specific polyketide analog from the culture. The method is most useful when the segment of the chromosome modified is involved in an enzymatic activity associated with polyketide biosynthesis, particularly for manipulating polyketide synthase genes from Saccarharopolyspora or Streptomyces.

28 Claims, 96 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 93

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 127. Document ID: US 5817502 A

L2: Entry 127 of 141 File: USPT Oct 6, 1998

US-PAT-NO: 5817502
DOCUMENT-IDENTIFIER: US 5817502 A

TITLE: Genes for the synthesis of pyrrolnitrin

DATE-ISSUED: October 6, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James M. | Apex | NC | | |
| Hill; Dwight Steven | Cary | NC | | |
| Lam; Stephen Ting | Raleigh | NC | | |
| Hammer; Philip E. | Cary | NC | | |
| van Pee; Karl-Heinz | Bannewitz | | | DE |
| Kirner; Sabine | Puchheim | | | DE |

US-CL-CURRENT: 435/252.34; 435/117, 435/252.3, 435/252.33, 435/320.1, 435/69.1, 435/71.1, 536/23.2, 536/23.7

ABSTRACT:

The present invention is directed to the production of an antipathogenic substance (APS) in a host via recombinant expression of the polypeptides needed to biologically synthesize the APS. Genes encoding polypeptides necessary to produce particular antipathogenic substances are provided, along with methods for identifying and isolating genes needed to recombinantly biosynthesize any desired APS. The cloned genes may be transformed and expressed in a desired host organisms to produce the APS according to the invention for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of the APS.

27 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 128. Document ID: US 5723759 A

L2: Entry 128 of 141 File: USPT Mar 3, 1998

US-PAT-NO: 5723759
DOCUMENT-IDENTIFIER: US 5723759 A

TITLE: Pyrrolnitrin biosynthesis genes

DATE-ISSUED: March 3, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James M. | Basel | | | CH |
| Hill; Dwight Steven | Cary | NC | | |
| Ryals; John Andrew | Durham | NC | | |
| Lam; Stephen Ting | Raleigh | NC | | |
| Hammer; Philip E. | Cary | NC | | |

US-CL-CURRENT: 800/301; 435/117, 435/252.3, 435/320.1, 435/69.1, 435/70.1, 536/23.2, 536/23.7

ABSTRACT:

The present invention is directed to the production of an antipathogenic substance (APS) in a host via recombinant expression of the polypeptides needed to biologically synthesize the APS. Genes encoding polypeptides necessary to produce particular antipathogenic substances are provided, along with methods for identifying and isolating genes needed to recombinantly biosynthesize any desired APS. The cloned genes may be transformed and expressed in a desired host organisms to produce the APS according to the invention for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of the APS.

8 Claims, 9 Drawing figures
Exemplary Claim Number: 1,6
Number of Drawing Sheets: 9



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☐ 129. Document ID: US 5716849 A

L2: Entry 129 of 141 File: USPT Feb 10, 1998

US-PAT-NO: 5716849
DOCUMENT-IDENTIFIER: US 5716849 A

TITLE: Genes for the biosynthesis of soraphen

DATE-ISSUED: February 10, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James M. | Apex | NC | | |
| Schupp; Thomas | Mohlin | | | CH |
| Beck; James J. | Cary | NC | | |
| Hill; Dwight S. | Cary | NC | | |
| Neff; Snezana | Bubendorf | | | CH |
| Ryals; John A. | Cary | NC | | |

US-CL-CURRENT: 435/419; 435/252.3, 435/252.31, 435/252.32, 435/252.33, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

The present invention is directed to the production of a polyketide antibiotic such as soraphen in a host via recombinant expression of the polypeptides needed to biologically synthesize the polyketide antibiotic. Polyketide synthase (PKS) genes encoding polypeptides necessary to synthesize soraphen are provided, along with methods for identifying and isolating the PKS genes needed to recombinantly biosynthesize any desired polyketide antibiotic. The cloned PKS genes may be transformed and expressed in a desired host organisms to produce soraphen for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of soraphen.

29 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 130. Document ID: US 5712146 A

L2: Entry 130 of 141 File: USPT Jan 27, 1998

US-PAT-NO: 5712146
DOCUMENT-IDENTIFIER: US 5712146 A
**** See image for Certificate of Correction ****

TITLE: Recombinant combinatorial genetic library for the production of novel polyketides

DATE-ISSUED: January 27, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB2 |
| Ebert-Khosla; Suzanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Fu; Hong | Stanford | CA | | |
| Kao; Camilla | Stanford | CA | | |

US-CL-CURRENT: 435/252.35; 435/148, 435/156, 435/252.3, 435/252.33, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

5 Claims, 33 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 131. Document ID: US 5698425 A

L2: Entry 131 of 141 File: USPT Dec 16, 1997

US-PAT-NO: 5698425
DOCUMENT-IDENTIFIER: US 5698425 A

TITLE: Method of protecting plants by transformation with genes for the synthesis of antipathogenic substances

DATE-ISSUED: December 16, 1997

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James M. | Basel | | | CH |
| Schupp; Thomas | Mohlin | | | CH |
| Beck; James Joseph | Cary | NC | | |
| Hill; Dwight Steven | Cary | NC | | |
| Ryals; John Andrew | Durham | NC | | |
| Lam; Stephen Ting | Raleigh | NC | | |
| Hammer; Philip E. | Cary | NC | | |
| Uknes; Scott Joseph | Apex | NC | | |

US-CL-CURRENT: 800/279; 435/117, 435/418, 435/419, 435/69.1, 435/70.1

ABSTRACT:

The present invention is directed to the production of an antipathogenic substance (APS) in a host via recombinant expression of the polypeptides needed to biologically synthesize the APS. Genes encoding polypeptides necessary to produce particular antipathogenic substances are provided, along with methods for identifying and isolating genes needed to recombinantly biosynthesize any desired APS. The cloned genes may be transformed and expressed in a desired host organisms to produce the APS according to the invention for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of the APS.

9 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 132. Document ID: US 5679560 A

L2: Entry 132 of 141 File: USPT Oct 21, 1997

US-PAT-NO: 5679560
DOCUMENT-IDENTIFIER: US 5679560 A

TITLE: Genes for the synthesis of antipathogenic substances

DATE-ISSUED: October 21, 1997

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James M. | Apex | NC | | |
| Hill; Dwight Steven | Cary | NC | | |
| Lam; Stephen Ting | Raleigh | NC | | |
| Hammer; Philip E. | Cary | NC | | |

US-CL-CURRENT: 435/183; 435/253.3, 435/41

ABSTRACT:

The present invention is directed to the production of an antipathogenic substance (APS) in a host via recombinant expression of the polypeptides needed to biologically synthesize the APS. Genes encoding polypeptides necessary to produce particular antipathogenic substances are provided, along with methods for identifying and isolating genes needed to recombinantly biosynthesize any desired APS. The cloned genes may be transformed and expressed in a desired host organisms to produce the APS

according to the invention for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of the APS.

13 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 133. Document ID: US 5672491 A

L2: Entry 133 of 141 File: USPT Sep 30, 1997

US-PAT-NO: 5672491
DOCUMENT-IDENTIFIER: US 5672491 A
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: September 30, 1997

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Khosla; Chaitan | Stanford | CA | | |
| Hopwood; David A. | Norwich | | | GB2 |
| Ebert-Khosla; Suzanne | Stanford | CA | | |
| McDaniel; Robert | Palo Alto | CA | | |
| Fu; Hong | Stanford | CA | | |
| Kao; Camilla | Stanford | CA | | |

US-CL-CURRENT: 435/148; 435/183, 435/252.35, 435/320.1, 435/76, 435/91.4

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

24 Claims, 15 Drawing figures
Exemplary Claim Number: 15
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 134. Document ID: US 5662898 A

L2: Entry 134 of 141 File: USPT Sep 2, 1997

US-PAT-NO: 5662898
DOCUMENT-IDENTIFIER: US 5662898 A
**** See image for Certificate of Correction ****

TITLE: Genes for the synthesis of antipathogenic substances

DATE-ISSUED: September 2, 1997

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James M. | Basel | | | CH |
| Schupp; Thomas | Mohlin | | | CH |
| Beck; James Joseph | Cary | NC | | |
| Hill; Dwight Steven | Cary | NC | | |
| Ryals; John Andrew | Durham | NC | | |
| Gaffney; Thomas Deane | Chapel Hill | NC | | |
| Lam; Stephen Ting | Raleigh | NC | | |
| Hammer; Philip E. | Cary | NC | | |
| Uknes; Scott Joseph | Apex | NC | | |

US-CL-CURRENT: 424/93.2; 435/252.3

ABSTRACT:

The present invention is directed to the production of an antipathogenic substance (APS) in a host via recombinant expression of the polypeptides needed to biologically synthesize the APS. Genes encoding polypeptides necessary to produce particular antipathogenic substances are provided, along with methods for identifying and isolating genes needed to recombinantly biosynthesize any desired APS. The cloned genes may be transformed and expressed in a desired host organisms to produce the APS according to the invention for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of the APS.

5 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 135. Document ID: US 5643774 A

L2: Entry 135 of 141 File: USPT Jul 1, 1997

US-PAT-NO: 5643774
DOCUMENT-IDENTIFIER: US 5643774 A
**** See image for Certificate of Correction ****

TITLE: Genes for the synthesis of antipathogenic substance

DATE-ISSUED: July 1, 1997

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James M. | Basel | | | CH |
| Schupp; Thomas | Mohlin | | | CH |
| Beck; James Joseph | Cary | NC | | |
| Hill; Dwight Steven | Cary | NC | | |
| Ryals; John Andrew | Durham | NC | | |
| Gaffney; Thomas Deane | Chapel Hill | NC | | |
| Lam; Stephen Ting | Raleigh | NC | | |
| Hammer; Philip E. | Cary | NC | | |
| Uknes; Scott Joseph | Apex | NC | | |

US-CL-CURRENT: 435/183; 435/69.1

ABSTRACT:

The present invention is directed to the production of an antipathogenic substance (APS) in a host via recombinant expression of the polypeptides needed to biologically synthesize the APS. Genes encoding polypeptides necessary to produce particular antipathogenic substances are provided, along with methods for identifying and isolating genes needed to recombinantly biosynthesize any desired APS. The cloned genes may be transformed and expressed in a desired host organisms to produce the APS according to the invention for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of the APS.

6 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 136. Document ID: US 5639949 A

L2: Entry 136 of 141 File: USPT Jun 17, 1997

US-PAT-NO: 5639949
DOCUMENT-IDENTIFIER: US 5639949 A

TITLE: Genes for the synthesis of antipathogenic substances

DATE-ISSUED: June 17, 1997

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Ligon; James M. | Basel | | | CH |
| Hill; Dwight Steven | Cary | NC | | |
| Ryals; John Andrew | Durham | NC | | |
| Lam; Stephen Ting | Raleigh | NC | | |
| Hammer; Philip E. | Cary | NC | | |

US-CL-CURRENT: 800/301; 435/117, 435/252.33, 435/252.34, 435/320.1, 435/69.1, 435/71.1, 536/23.2, 536/23.7

ABSTRACT:

The present invention is directed to the production of an antipathogenic substance (APS) in a host via recombinant expression of the polypeptides needed to biologically

synthesize the APS. Genes encoding polypeptides necessary to produce particular antipathogenic substances are provided, along with methods for identifying and isolating genes needed to recombinantly biosynthesize any desired APS. The cloned genes may be transformed and expressed in a desired host organisms to produce the APS according to the invention for a variety of purposes, including protecting the host from a pathogen, developing the host as a biocontrol agent, and producing large, uniform amounts of the APS.

7 Claims, 9 Drawing figures
Exemplary Claim Number: 2,3,4
Number of Drawing Sheets: 9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 137. Document ID: US 5252474 A

L2: Entry 137 of 141 File: USPT Oct 12, 1993

US-PAT-NO: 5252474
DOCUMENT-IDENTIFIER: US 5252474 A

TITLE: Cloning genes from Streptomyces avermitilis for avermectin biosynthesis and the methods for their use

DATE-ISSUED: October 12, 1993

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Gewain; Keith M. | Middelsex | NJ | | |
| MacNeil; Douglas J. | Westfield | NJ | | |
| MacNeil; Tanya | Westfield | NJ | | |
| Paress; Philip S. | Maplewood | NJ | | |
| Ruby; Carolyn L. | Montclair | NJ | | |
| Streicher; Stanley L. | Verona | NJ | | |

US-CL-CURRENT: 435/91.1; 435/119, 435/252.33, 435/252.35, 435/320.1, 435/486, 435/488, 435/489, 435/76

ABSTRACT:

There are disclosed plasmids containing DNA isolated from Streptomyces avermitilis, the microorganism which is used to prepare avermectin compounds, identified as pAT1, pVE650 pVE855, pVE859, pVE1446, pVE923, and pVE924 which contain the genetic information for the biosynthesis of the avermectins. Methods for the isolation of such plasmid and for the manipulation of the plasmids to alter the formation of the avermectin compound are also disclosed.

46 Claims, 7 Drawing figures
Exemplary Claim Number: 24
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 138. Document ID: EP 997528 A1

L2: Entry 138 of 141 File: EPAB May 3, 2000

PUB-NO: EP000997528A1
DOCUMENT-IDENTIFIER: EP 997528 A1
TITLE: Streptomyces avermitilis regulatory genes for increased avermectin production

PUBN-DATE: May 3, 2000

INVENTOR-INFORMATION:

| NAME | COUNTRY |
|---|---|
| STUTZMAN-ENGWALL, KIM JONELLE | US |
| PRICE, BRENDA SUE | US |

INT-CL (IPC): C12 N 15/31; C12 N 15/76
EUR-CL (EPC): C12P019/62; C07K014/36, C12N015/01 , C12N015/76

ABSTRACT:

CHG DATE=20001128 STATUS=O> The present invention is directed to compositions and methods for producing avermectins, and is primarily in the field of animal health. The present invention relates to the identification and characterization of two novel genes, herein referred to as the aveR1 and aveR2 genes, that are involved in regulating avermectin polyketide synthase (PKS) expression and avermectin biosynthesis in Streptomyces avermitilis. The present invention is based on the discovery that inactivation of these genes results in an increase in the amount of avermectin produced by S. avermitilis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 139. Document ID: WO 200268613 A1

L2: Entry 139 of 141 File: DWPI Sep 6, 2002

DERWENT-ACC-NO: 2002-732747
DERWENT-WEEK: 200279
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TITLE: Genetic modification of microbial host cells for producing polyketide comprises the use of the enzymes which catalyze the production of starter and extender units

INVENTOR: KHOSLA, C; PFEIFER, B

PRIORITY-DATA: 2002US-355211P (February 8, 2002), 2001US-0798033 (February 28, 2001)

PATENT-FAMILY:

| PUB-NO | PUB-DATE | LANGUAGE | PAGES | MAIN-IPC |
|---|---|---|---|---|
| WO 200268613 A1 | September 6, 2002 | E | 080 | C12N001/21 |

INT-CL (IPC): C12 N 1/21; C12 N 9/00; C12 N 15/54; C12 N 15/63; C12 N 15/81

ABSTRACTED-PUB-NO: WO 200268613A
BASIC-ABSTRACT:

NOVELTY - Genetic modification (M1) of microbial host cells comprising incorporation of at least one expression system for producing a protein that catalyzes the production of starter and/or extender units and/or disabling at least one endogenous pathway for catabolism of starter and/or extender units, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) assessing (M2) the results of a procedure effecting modification of polyketide synthase genes, resulting in a mixture of the modified genes involving transfecting a culture of the microbial host cells (preferably E.coli) with the mixture of modified genes, culturing individual colonies of the transformed E.coli and assessing each colony for polyketide production;

(2) determining (M3) whether a substituted benzoate can prime an adenylation-thiolation (A-T) didomain of a rafamycin synthetase involving incubating a substituted benzoate with a holo A-T didomain for priming the A-T didomain and measuring the amount or presence of the substituted benzoate that primed the A-T didomain;

(3) prokaryotic host cells which do not produce the polyketide in the absence of genetic modification and are genetically modified for enhanced synthesis of at least one hybrid polyketide. The genetic modification involves incorporation of at least one expression system comprising an A-T didomain, which incorporates the starter unit that primes an A-T didomain according to (II);

(4) a hybrid polyketide in which the starter unit is incorporated in it;

(5) producing (M4) the polyketide involving culturing the microbial/prokaryotic cells;

(6) enhancing (M5) the production of at least one hybrid polyketide in the microbial host involving providing the host with an expression system for producing a protein that incorporates an exogenous starter unit that primes an A-T didomain according to (II);

(7) enhancing production of the secondary metabolite (preferably the polyketide) in a microbial host cell involving either inducing the production of the secondary metabolite after the microbial cells have reached a high cell density in the culture or maintaining the nutrient level fed to the microbe at a relatively constant level during the production of the secondary metabolite; and

(8) enhancing the production of the polyketide in a microbe involving modifying the microbe to contain an expression system for a thioesterase II (TEII).

USE - (M1) is useful for producing at least one polyketide and a complete polyketide derived from rifamycin, rapamycin, FK506, ansatrienin, FK520, microcystin, pimaricin, erythromycin, oleandomycin, megalomycin, picromycin, spinosad, avermectin, tylosin or epothilone (preferably a modified rifamycin or a 6-dEB analog) (claimed).

ADVANTAGE - The production of the polyketide and other secondary metabolite can be enhanced in microbial organisms. (M1) also results in a host organism with desirable characteristics to be used in the production of polyketides and to assess the results of gene shuffling.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

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☐ 140. Document ID: AU 758329 B AU 9947575 A JP 2000102394 A EP 997528 A1 CA 2281935 A1 CN 1252440 A CZ 9903232 A3 HU 9903073 A2 BR 9904109 A KR 2000023111 A US 6197591 B1 MX 9908462 A1 ZA 9905872 A KR 343357 B

L2: Entry 140 of 141 File: DWPI Mar 20, 2003

DERWENT-ACC-NO: 2000-318250
DERWENT-WEEK: 200329
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TITLE: Novel streptomyces avermitilis regulatory genes which when mutated are useful for increased production of avermectin useful as highly active parasitic agent for treating humans against parasite infections

INVENTOR: PRICE, B S; STUTZMAN-ENGWALL, K J

PRIORITY-DATA: 1998US-100134P (September 14, 1998), 1999US-0390721 (September 7, 1999)

PATENT-FAMILY:

| PUB-NO | PUB-DATE | LANGUAGE | PAGES | MAIN-IPC |
|---|---|---|---|---|
| AU 758329 B | March 20, 2003 | | 000 | C12N015/31 |
| AU 9947575 A | March 23, 2000 | | 065 | C12N015/31 |
| JP 2000102394 A | April 11, 2000 | | 040 | C12N015/09 |
| EP 997528 A1 | May 3, 2000 | E | 000 | C12N015/31 |
| CA 2281935 A1 | March 14, 2000 | E | 000 | C12N015/11 |
| CN 1252440 A | May 10, 2000 | | 000 | C12N001/21 |
| CZ 9903232 A3 | July 12, 2000 | | 000 | C12N001/20 |
| HU 9903073 A2 | July 28, 2000 | | 000 | C12N015/31 |
| BR 9904109 A | October 17, 2000 | | 000 | C12P019/62 |
| KR 2000023111 A | April 25, 2000 | | 000 | C12N015/31 |
| US 6197591 B1 | March 6, 2001 | | 000 | C12N015/76 |
| MX 9908462 A1 | March 1, 2000 | | 000 | C12N015/57 |
| ZA 9905872 A | May 31, 2001 | | 070 | C12N000/00 |
| KR 343357 B | July 15, 2002 | | 000 | C12N015/31 |

INT-CL (IPC): A01 K 0/00; A01 N 63/02; A61 K 31/70; A61 K 31/7056; A61 K 48/00; C07 H 21/00; C07 K 14/195; C07 K 14/36; C07 K 16/12; C12 N 0/00; C12 N 1/15; C12 N 1/19; C12 N 1/20; C12 N 1/21; C12 N 5/10; C12 N 15/01; C12 N 15/09; C12 N 15/11; C12 N 15/31; C12 N 15/57; C12 N 15/63; C12 N 15/76; C12 P 19/34; C12 P 19/62; C12 P 21/02; C12 P 21/08; C12 Q 1/68; C12 R 1/465; G01 N 33/15; G01 N 33/50; G01 N 33/569; G01 N 33/577; C12 P 19/62; C12 R 1:465; C12 N 15/31; C12 R 1:465; C12 N 1/21; C12 N 15/09; C12 P 21/02; C12 R 1:465; C12 R 1:465; C12 R 1:465

ABSTRACTED-PUB-NO: AU 9947575A
BASIC-ABSTRACT:

NOVELTY - Isolated polynucleotide molecule (I) encoding aveR1 gene and aveR2 gene products from Streptomyces avermitilis, is new.

DETAILED DESCRIPTION - Isolated polynucleotide molecule (I) encoding aveR1 gene and aveR2 gene products from Streptomyces avermitilis has a defined nucleotide sequence of 5045 base pairs given in the specification. The aveR1 gene product has a protein sequence of 401 amino acids (aa) and is encoded by an open reading frame (ORF) of nucleotides 1112 to 2317 of (I). The aveR2 gene product has a protein sequence of 235 aa and is encoded by an ORF of nucleotides 2314 to 3021 of (I).

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide molecule (Ia) homologous to a polynucleotide molecule comprising nucleotides 1112 to 2317 of (I);

(2) an isolated polynucleotide sequence (Ib) that naturally flanks the aveR1 open reading frame (ORF) of S. avermitilis in situ comprising nucleotides 1-1111 and 2318-5045 of (I);

(3) an isolated polynucleotide molecule (Ic) homologous to a polynucleotide molecule comprising nucleotides 2314 to 3021 of (I);

(4) an isolated polynucleotide sequence (Id) that naturally flanks the aveR2 open reading frame (ORF) of S. avermitilis in situ comprising nucleotides 1-2313 and 3022-5045 of (I);

(5) an oligonucleotide molecule that hybridizes under highly stringent conditions to a polynucleotide comprising (I) or the complement of (I);

(6) a recombinant vector (II) comprising (I);

(7) a transformed host cell (III) comprising (II);

(8) a substantially purified or isolated polypeptide (IV) comprising a sequence of 401 or 235 amino acids (as given in the specification), its homologous polypeptides or their fragments;

(9) preparation (P1) of (IV);

(10) a polynucleotide molecule (Ie) comprising (I) with at least one mutation that results in a detectable increase in the amount of avermectins produced by the cells of a strain of S. avermitilis compared to the cells of same strain that do not carry the gene mutation;

(11) a genetic construct (GC) comprising (Ie) for introducing a mutation into either or both of the aveR genes;

(12) identifying a mutation in the aveR genes in a species or strain of S. avermitilis by comparing the amounts of avermectin produced by mutant and non-mutant strains and detecting the mutation from the increased amount of avermectins produced by the mutant strains;

(13) preparation (P2) of genetically modified cells of S. avermitilis;

(14) a strain of Streptomyces, producing increased amount of avermectins as a result of mutation in aveR genes; and

(15) an antibody (Ab) directed against aveR1 or aveR2 gene product.

ACTIVITY - Antiparasitic; insecticide.

MECHANISM OF ACTION - Avermectin polyketide synthase regulator. No supporting data given.

USE - (I) is useful for increased production of avermectins which comprises culturing the cells of species or strains of Streptomyces comprising mutated averR genes (claimed). (Ie) is useful to mutate aveR genes (claimed). Avermectins are highly active anti parasitic agents having particular utility as anthelmintics, ectoparasiticides, insecticides and acaricides and useful for treating various diseases or conditions in humans, particularly those caused by parasitic infections.

ADVANTAGE - Avermectins prepared are effective against various nematodes, parasites including gastrointestinal parasites, ectoparasites, insects and other organisms, thus providing a wide range of treatment.
ABSTRACTED-PUB-NO:

US 6197591B EQUIVALENT-ABSTRACTS:

NOVELTY - Isolated polynucleotide molecule (I) encoding aveR1 gene and aveR2 gene products from Streptomyces avermitilis, is new.

DETAILED DESCRIPTION - Isolated polynucleotide molecule (I) encoding aveR1 gene and aveR2 gene products from Streptomyces avermitilis has a defined nucleotide sequence of 5045 base pairs given in the specification. The aveR1 gene product has a protein sequence of 401 amino acids (aa) and is encoded by an open reading frame (ORF) of nucleotides 1112 to 2317 of (I). The aveR2 gene product has a protein sequence of 235 aa and is encoded by an ORF of nucleotides 2314 to 3021 of (I).

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide molecule (Ia) homologous to a polynucleotide molecule comprising nucleotides 1112 to 2317 of (I);

(2) an isolated polynucleotide sequence (Ib) that naturally flanks the aveR1 open reading frame (ORF) of S. avermitilis in situ comprising nucleotides 1-1111 and 2318-5045 of (I);

(3) an isolated polynucleotide molecule (Ic) homologous to a polynucleotide molecule comprising nucleotides 2314 to 3021 of (I);

(4) an isolated polynucleotide sequence (Id) that naturally flanks the aveR2 open reading frame (ORF) of S. avermitilis in situ comprising nucleotides 1-2313 and

3022-5045 of (I);

(5) an oligonucleotide molecule that hybridizes under highly stringent conditions to a polynucleotide comprising (I) or the complement of (I);

(6) a recombinant vector (II) comprising (I);

(7) a transformed host cell (III) comprising (II);

(8) a substantially purified or isolated polypeptide (IV) comprising a sequence of 401 or 235 amino acids (as given in the specification), its homologous polypeptides or their fragments;

(9) preparation (P1) of (IV);

(10) a polynucleotide molecule (Ie) comprising (I) with at least one mutation that results in a detectable increase in the amount of avermectins produced by the cells of a strain of S. avermitilis compared to the cells of same strain that do not carry the gene mutation;

(11) a genetic construct (GC) comprising (Ie) for introducing a mutation into either or both of the aveR genes;

(12) identifying a mutation in the aveR genes in a species or strain of S. avermitilis by comparing the amounts of avermectin produced by mutant and non-mutant strains and detecting the mutation from the increased amount of avermectins produced by the mutant strains;

(13) preparation (P2) of genetically modified cells of S. avermitilis;

(14) a strain of Streptomyces, producing increased amount of avermectins as a result of mutation in aveR genes; and

(15) an antibody (Ab) directed against aveR1 or aveR2 gene product.

ACTIVITY - Antiparasitic; insecticide.

MECHANISM OF ACTION - Avermectin polyketide synthase regulator. No supporting data given.

USE - (I) is useful for increased production of avermectins which comprises culturing the cells of species or strains of Streptomyces comprising mutated averR genes (claimed). (Ie) is useful to mutate aveR genes (claimed). Avermectins are highly active anti parasitic agents having particular utility as anthelmintics, ectoparasiticides, insecticides and acaricides and useful for treating various diseases or conditions in humans, particularly those caused by parasitic infections.

ADVANTAGE - Avermectins prepared are effective against various nematodes, parasites including gastrointestinal parasites, ectoparasites, insects and other organisms, thus providing a wide range of treatment.



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| Terms | Documents |
|---|---|
| l1 and (nucleic acid or gene or dna or cdna) | 141 |

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**Search Results** - Record(s) 141 through 141 of 141 returned.

☐ 141. Document ID: WO 200001827 A2 JP 2002519066 W AU 9946365 A BR 9911898 A EP 1095147 A2 CN 1316002 A CZ 200100023 A3 KR 2001074652 A ZA 200100775 A HU 200105464 A2

L2: Entry 141 of 141 File: DWPI Jan 13, 2000

DERWENT-ACC-NO: 2000-182117
DERWENT-WEEK: 200246
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TITLE: Mutated Type I polyketide synthase containing a polylinker site in an extension module for replacement of a reductive loop sequence, for producing polyketides, e.g. B1 avermectin

INVENTOR: KELLENBERGER, J L; LEADLAY, P F ; MCARTHUR, H A I ; STAUNTON, J ; STUTZMAN-ENGWALL, K J

PRIORITY-DATA: 1998GB-0014622 (July 6, 1998)

PATENT-FAMILY:

| PUB-NO | PUB-DATE | LANGUAGE | PAGES | MAIN-IPC |
|---|---|---|---|---|
| WO 200001827 A2 | January 13, 2000 | E | 075 | C12N015/52 |
| JP 2002519066 W | July 2, 2002 | | 070 | C12N015/09 |
| AU 9946365 A | January 24, 2000 | | 000 | C12N015/52 |
| BR 9911898 A | March 27, 2001 | | 000 | C12N015/52 |
| EP 1095147 A2 | May 2, 2001 | E | 000 | C12N015/52 |
| CN 1316002 A | October 3, 2001 | | 000 | C12N015/52 |
| CZ 200100023 A3 | December 12, 2001 | | 000 | C12N015/52 |
| KR 2001074652 A | August 4, 2001 | | 000 | C12N015/54 |
| ZA 200100775 A | January 30, 2002 | | 088 | C12N000/00 |
| HU 200105464 A2 | April 29, 2002 | | 000 | C12N015/52 |

INT-CL (IPC): C07 K 19/00; C12 N 0/00; C12 N 1/21; C12 N 9/02; C12 N 9/04; C12 N 9/10; C12 N 9/88; C12 N 15/09; C12 N 15/52; C12 N 15/54; C12 N 15/62; C12 P 17/06; C12 P 19/62; C12 N 1/21; C12 R 1:465

ABSTRACTED-PUB-NO: WO 200001827A
BASIC-ABSTRACT:

NOVELTY - Nucleic acid molecule (I) encoding (part of) a Type I polyketide synthase comprising (part of) an extension module, with a polylinker comprising multiple restriction sites replacing at least 1 gene encoding an enzyme associated with reduction, or a polylinker that connects nucleic acids encoding (part of) an acyltransferase enzyme and (part of) an acyl carrier protein, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a vector including (I);

(2) a host cell transfected, transformed or conjugated with (I) or the vector of (1);

(3) producing a nucleic acid encoding a novel polyketide synthase by incorporating a nucleic acid sequence encoding at least one reductive enzyme into (I);

(4) producing a fermentation product containing a polyketide synthase by culturing the host cell of (2);

(5) a fermentation product containing a C22-C23 dihydroavermectin (especially ivermectin) substantially free of other macrolides;

(6) a fermentation product containing a B1 avermectin free of B2 avermectins.

ACTIVITY - Antibiotic; insecticide.

MECHANISM OF ACTION - None given.

USE - The nucleic acids and methods for producing fermantation products are used to prepare polyketides by replacing the reductive loop in a selected module of a Type I polyketide synthase with the equivalent segment from the same or different polyketide synthase gene cluster or by a mutated or synthetic segment. The polyketides produced are useful as antibiotics and insecticides.



| Terms | Documents |
|---|---|
| l1 and (nucleic acid or gene or dna or cdna) | 141 |

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**Search Results** - Record(s) 1 through 1 of 1 returned.

☐ 1. Document ID: EP 1160325 A1

L3: Entry 1 of 1 File: EPAB Dec 5, 2001

PUB-NO: EP001160325A1
DOCUMENT-IDENTIFIER: EP 1160325 A1
TITLE: AVERMECTIN AGLYCON SYNTHASE GENES

PUBN-DATE: December 5, 2001

INVENTOR-INFORMATION:

| NAME | COUNTRY |
|---|---|
| OMURA, SATOSHI | JP |
| IKEDA, HARUO | JP |

INT-CL (IPC): C12 N 15/52; C12 N 1/21; C12 N 9/00; C12 N 9/88; C12 P 19/62
EUR-CL (EPC): C12P019/62; C12N015/52

ABSTRACT:

CHG DATE=20020103 STATUS=O> The present invention relates to an isolated DNA which comprises a DNA sequence encoding avermectin aglycon synthase domains that corresponds to multifunctional enzyme proteins involved in the biosynthesis of a polyketide compound, or its mutants having avermectin aglycon synthase activity, particularly functional modules and submodules in the DNA sequence derived from Streptomyces avermitilis, a polypeptide or mutants thereof encoded by the DNA or the mutants, a vector containing the DNA or the mutants, a host cell transformed with the DNA, the mutants thereof, or the vector, and a method for producing avermectin.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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| Terms | Documents |
|---|---|
| avermectin aglycon synthase | 1 |

**Display Format:** - Change Format

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**Search Results** - Record(s) 1 through 12 of 12 returned.

☐ 1. Document ID: US 5411737 A

L4: Entry 1 of 12 File: USPT May 2, 1995

US-PAT-NO: 5411737
DOCUMENT-IDENTIFIER: US 5411737 A

TITLE: Slow release syneresing polymeric drug delivery device

DATE-ISSUED: May 2, 1995

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Hsu; Terry T. | North Wales | PA | | |
| Michaels; Alan S. | Chestnut Hill | MA | | |

US-CL-CURRENT: 424/411; 424/405, 424/486

ABSTRACT:

There is disclosed a slow release drug delivery device for the prolonged administration of topically active medicines which consists of a vehicle in which water is soluble and in which is dissolved the topically active drug which is formed into a stable organogel with a polymer matrix with a very low water absorbing capability. The organogel, in the presence of water or atmospheric water vapor, slowly imbibes such water into the vehicle and by doing so the vehicle becomes incompatible with the matrix and is slowly expelled therefrom. The vehicle dissolves the drug and the vehicle/drug combination is slowly pumped out of the polymeric matrix with substantially linear drug delivery occurring for periods in excess of 6 months. The drug delivery device may be used to administer drugs topically, as a collar or trans dermal patch, orally, as a slow delivery device, particularly as a ruminal bolus, or as a suppository or a subcutaneous implant. The preferred form for the drug delivery device is as a flea and tick collar for household pets and the preferred active drug is selected from the avermectin and milbemycin families of active antiparasitic agents.

27 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 2. Document ID: US 5122618 A

L4: Entry 2 of 12 File: USPT Jun 16, 1992

US-PAT-NO: 5122618
DOCUMENT-IDENTIFIER: US 5122618 A

TITLE: Insecticides and parasiticides

DATE-ISSUED: June 16, 1992

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| O'Sullivan; Anthony C. | Basel | | | CH |

US-CL-CURRENT: 549/264

ABSTRACT:

The present invention relates to novel derivatives of formula I that can be derived from milbemycins, to their preparation and their use for controlling pests, and also to pesticides that contain at least one of these compounds as active ingredient.

The novel compounds have the general formula I ##STR1## in which X is one of the groups --CH(OR.sub.1)--, --C(O)-- or --C(.dbd.N--OR)--;

R.sub.1 is hydrogen or an OH-protecting group;

R is hydrogen, an OH-protecting group, or an alkyl or cycloalkyl group;

R.sub.2 is methyl, ethyl, isopropyl or sec.-butyl; and

Ph is a phenyl ring that is substituted by R.sub.a, R.sub.b, R.sub.c and R.sub.d, wherein each of R.sub.a, R.sub.b, R.sub.c and R.sub.d, independently of the others, is hydrogen, C.sub.1 -C.sub.10 alkyl, C.sub.2 -C.sub.10 alkoxyalkyl, C.sub.2 -C.sub.10 alkenyl, C.sub.1 -C.sub.10 alkoxy, C.sub.2 -C.sub.10 alkoxyalkoxy, or a phenyl or phenoxy radical that is unsubstituted or is substituted by at least one substituent from the group C.sub.1 -C.sub.3 alkyl and C.sub.1 -C.sub.3 alkoxy.

3 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 3. Document ID: US 5077308 A

L4: Entry 3 of 12 File: USPT Dec 31, 1991

US-PAT-NO: 5077308
DOCUMENT-IDENTIFIER: US 5077308 A

TITLE: Avermectin ketal derivatives useful as antiparasitic

DATE-ISSUED: December 31, 1991

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Blizzard; Timothy A. | Rahway | NJ | | |

US-CL-CURRENT: 514/450; 549/264, 549/265

ABSTRACT:

There are disclosed avermectin aglycone derivatives which incorporate a ketal at position 13. The synthetic ketal analogs are derived from the corresponding ketones which in turn are prepared by chemical modification of naturally occurring avermectins. The compounds are active antiparasitic agents and compositions for that use are disclosed.

16 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 4. Document ID: US 4959386 A

L4: Entry 4 of 12 File: USPT Sep 25, 1990

US-PAT-NO: 4959386
DOCUMENT-IDENTIFIER: US 4959386 A

TITLE: Pesticides

DATE-ISSUED: September 25, 1990

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Frei; Bruno | Liestal | | | CH |
| Mereyala; Hari B. | Pune | | | IN |
| O'Sullivan; Anthony C. | Basel | | | CH |
| Sato; Kazuo | Kanagawa | | | CH |
| Yanai; Toshiaki | Kanagawa | | | CH |

US-CL-CURRENT: 514/450; 549/264

ABSTRACT:

The present invention relates to novel compounds of the formula ##STR1## wherein R.sub.1 is hydrogen, a silyl group or an acyl group,

R.sub.2 is methyl, ethyl, is propyl or sec-butyl, and R is hydrogen, unsubstituted or substituted straight chain or branched C.sub.1 -Cl.sub.18 alkyl, an unsubstituted or substituted cycloaliphatic group containing 3 to 10 carbon atoms, unsubstituted or substituted C.sub.2 -C.sub.6 alkenyl, unsubstituted or substituted C.sub.2 -C.sub.6 -alkynyl, unsubstituted or substituted phenyl or unsubstituted or substituted benzyl. These compounds posseses advantageous pesticidal properties and are suitable in particular for controlling pests in agriculture and the storage sector.

7 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 5. Document ID: US 4954484 A

L4: Entry 5 of 12 File: USPT Sep 4, 1990

US-PAT-NO: 4954484
DOCUMENT-IDENTIFIER: US 4954484 A

TITLE: Parasiticides and insecticides

DATE-ISSUED: September 4, 1990

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Gehret; Jean-Claude | Aesch | | | CH |

US-CL-CURRENT: 514/30; 514/450, 536/7.1, 549/264

ABSTRACT:

Novel compounds of formula ##STR1## in which A is a ##STR2## group wherein R.sub.1 is hydrogen or an OH-protecting group, and R.sub.11 is hydrogen, an OH-protecting group, or an alkyl, cycloalkyl or acyl group,

R.sub.2 is methyl, ethyl, isopropyl, sec.-butyl or a --C(CH.sub.3).dbd.CH--E group wherein E is methyl, ethyl or isopropyl,

R.sub.3 and R.sub.4 together represent a bond between the two carbon atoms to which they are bonded, or together represent a --C(X')(Z')-- group wherein X' and Z' each represents, independently of the other, hydrogen or halogen, and

X and Z each represents, independently of the other, hydrogen or halogen,

the preparation of the novel compounds and the use thereof for controlling parasites of productive livestock and for controlling harmful insects.

13 Claims, 0 Drawing figures
Exemplary Claim Number: 1,13



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☐ 6. Document ID: US 4920148 A

L4: Entry 6 of 12 File: USPT Apr 24, 1990

US-PAT-NO: 4920148
DOCUMENT-IDENTIFIER: US 4920148 A

TITLE: Insecticides and parasiticides

DATE-ISSUED: April 24, 1990

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Gehret; Jean-Claude | Aesch | | | CH |

US-CL-CURRENT: 514/450; 514/63, 549/214, 549/264

ABSTRACT:

The present invention relates to novel C(29)-oximinomilbemycin derivatives of formula I, to their preparation and to the use thereof for controlling pests. The invention further relates to pesticidal compositions which contain at least one of these compounds as active ingredient.

The novel compounds have the general formula I ##STR1## wherein X is a group selected from --CH(OR.sub.1)--, --C(O)--or --C(.dbd.N--OR)--,

R.sub.1 is hydrogen or a OH protective group,

R is hydrogen, a OH protective group, an alkyl, cycloakyl or acyl group,

R.sub.2 is methyl, ethyl, isopropyl, sec-butyl or the ##STR2## group, wherein A is methyl, ethyl or isopropyl; and R.sub.3 is hydrogen, C.sub.1 -C.sub.6 alkyl, C.sub.2 -C.sub.6 alkenyl, a radical selected from the group consisting of phenyl and benzyl which is unsubstituted or substituted by one or more members selected from the group consisting of halogen, C.sub.1 -C.sub.3 alkyl, C.sub.1 -C.sub.3 alkoxy, C.sub.1 -C.sub.3 alkylthio, C.sub.1 -C.sub.3 haloalkyl, nitro or cyano, or is the group U ##STR3## wherein n is 0, 1, 2, 3, 4 or 5, E is oxygen or --CH(R.sub.d)-- and R.sub.z is hydrogen, R.sub.a is hydrogen, halogen, C.sub.1 -C.sub.3 alkyl, C.sub.1 -C.sub.3 alkoxy or 2-tetrahydropyranyl, and R.sub.b, R.sub.c and R.sub.d are each independently hydrogen, halogen, C.sub.1 -C.sub.3 alkyl or C.sub.1 -C.sub.3 alkoxy, which group U may also be in unsaturated form.

11 Claims, 0 Drawing figures
Exemplary Claim Number: 1,9



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☐ 7. Document ID: US 4918097 A

L4: Entry 7 of 12 File: USPT Apr 17, 1990

US-PAT-NO: 4918097
DOCUMENT-IDENTIFIER: US 4918097 A

TITLE: Insecticides and parasiticides

DATE-ISSUED: April 17, 1990

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| O'Sullivan; Anthony C. | Basel | | | CH |

US-CL-CURRENT: 514/450; 549/214, 549/264, 549/265

ABSTRACT:

The present invention relates to novel derivatives of formula I that can be derived from milbemycins, to their preparation and their use for controlling pests, and also to pesticides that contain at least one of these compounds as active ingredient.

The novel compounds have the general formula I ##STR1## in which X is one of the groups --CH(OR.sub.1)--, --C(O)-- or --C(=N--OR)--;

R.sub.1 is hydrogen or an OH-protecting group;

R is hydrogen, an OH-protecting group, or an alkyl or cycloalkyl group;

R.sub.2 is methyl, ethyl, isopropyl or sec.-butyl;

and

Ph is a phenyl ring that is substituted by R.sub.a, R.sub.b, R.sub.c and R.sub.d, wherein each of R.sub.a, R.sub.b, R.sub.c and R.sub.d, independently of the others, is hydrogen, C.sub.1 -C.sub.10 alkyl, C.sub.2 -C.sub.10 alkoxyalkyl, C.sub.2 -C.sub.10 alkenyl, C.sub.1 -C.sub.10 alkoxy, C.sub.2 -C.sub.10 alkoxyalkoxy, or a phenyl or phenoxy radical that is unsubstituted or is substituted by at least one substituent from the group C.sub.1 -C.sub.3 alkyl and C.sub.1 -C.sub.3 alkoxy.

18 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 8. Document ID: US 4897416 A

L4: Entry 8 of 12 File: USPT Jan 30, 1990

US-PAT-NO: 4897416
DOCUMENT-IDENTIFIER: US 4897416 A

TITLE: Insecticides and parasiticides

DATE-ISSUED: January 30, 1990

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Frei; Bruno | Liestal | | | CH |
| Sullivan; Anthony C. | Basel | | | CH |

US-CL-CURRENT: 514/450; 549/264

ABSTRACT:

The present invention relates to novel 5-oximino-13.beta.-carbonylthiomilbemycin derivatives of formula I, to their preparation and to the use thereof for controlling pests. The invention further relates to pesticidal compositions which contain at least one of these compounds as active ingredient. The novel compounds have the general formula I ##STR1## wherein R.sub.1 is hydrogen or an alkyl, cycloalkyl or acyl group,

R.sub.2 is methyl, ethyl, isopropyl or sec-butyl, or is the ##STR2## group, wherein X is methyl, ehtyl or isopropyl, and R is hydrogen or an unsubstituted or substituted straight chain or branched C.sub.1 -C.sub.18 alkyl group, an unsubstituted or substituted cycloaliphatic group of 3 to 10 carbon atoms, an unsubstituted or substituted C.sub.2 -C.sub.6 alkenyl group, an unsubstituted or substituted C.sub.2 -C.sub.6 alkynyl group, an unsubstituted or substituted phenyl group or an unsubstituted or substituted benzyl group.

14 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 9. Document ID: US 4855317 A

L4: Entry 9 of 12 File: USPT Aug 8, 1989

US-PAT-NO: 4855317
DOCUMENT-IDENTIFIER: US 4855317 A

TITLE: Insecticides and parasiticides

DATE-ISSUED: August 8, 1989

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Gehret; Jean-Claude | Aesch | | | CH |

US-CL-CURRENT: 514/450; 549/264

ABSTRACT:

The present invention relates to novel C(29)-oximinomilbemycin derivatives of formula I, to their preparation and to the use thereof for controlling pests. The invention further relates to pesticidal compositions which contain at least one of these compounds as active ingredient.

The novel compounds have the general formula I ##STR1## wherein X is a group selected from --CH(OR.sub.1)--, --C(O)-- or --C(.dbd.N--OR)--,

R.sub.1 is hydrogen or a OH protective group,

R is hydrogen, a OH protective group, an alkyl, cycloalkyl or acyl group,

R.sub.2 is methyl, ethyl, isopropyl, sec-butyl or the ##STR2## wherein A is methyl, ethyl or isopropyl; and R.sub.3 is hydrogen, C.sub.1 -C.sub.6 alkyl, C.sub.2 -C.sub.6 alkenyl, a radial selected from the group consisting of phenyl and benzyl which is unsubstituted or substituted by one or more members selected from the group consisting of halogen, C.sub.1 -C.sub.3 alkyl, C.sub.1 -C.sub.3 alkoxy, C.sub.1 -C.sub.3 alkylthio, C.sub.1 -C.sub.3 haloalkyl, nitro or cyano, or is the group U ##STR3## wherein n is 0, 1, 2, 3, 4 or 5, E is oxygen or --CH(R.sub.d)-- and R.sub.z is hydrogen, R.sub.a is hydrogen, halogen, C.sub.1 -C.sub.3 alkyl, C.sub.1 -C.sub.3 alkoxy or 2-tetrahydropyranyl, and R.sub.b, R.sub.c and R.sub.d are each independently hydrogen, halogen, C.sub.1 -C.sub.3 alkyl or C.sub.1 -C.sub.3 alkoxy, which group U may also be in unsaturated form.

14 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 10. Document ID: US 4696922 A

L4: Entry 10 of 12 File: USPT Sep 29, 1987

US-PAT-NO: 4696922
DOCUMENT-IDENTIFIER: US 4696922 A

TITLE: 5-azolylacetoxymilbemycins as ecto- and endoparasites

DATE-ISSUED: September 29, 1987

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Sturm; Elmar | Aesch | | | CH |
| Maienfisch; Peter | Aesch | | | CH |

US-CL-CURRENT: 514/185; 514/359, 514/382, 514/383, 514/397, 514/407, 548/101, 548/253, 548/255, 548/266.4, 548/300.7, 548/341.5, 548/357.5, 548/376.1, 549/264

ABSTRACT:

The present invention relates to milbemycin derivatives of the formula I ##STR1## wherein X is hydrogen or .beta.-halogen, R is methyl, ethyl, isopropyl or sec-butyl and Az is a 5 membered heterocyclic aromatic ring which contains 2-4 nitrogen atoms and is

attached in the 1-position and which is unsubstituted or substituted by one or two C.sub.1 -C.sub.6 alkyl groups. These compounds, and the acid addition salts and metal complexes thereof, are effective pesticides for controlling endo-and ectoparasites, especially for controlling neamatodes which are parasites of animals. The may be obtained by appropriate esterification in 5-position of milbemycin derivatives. The selective .beta.-halogenation of 14,15-epoxymilbemycin derivatives can be effected via the intermediate .DELTA..sup.13,14 -15-hydroxymilbemycins with appropriate halogenating agents.

16 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 11. Document ID: JP 2000245457 A

L4: Entry 11 of 12 File: JPAB Sep 12, 2000

PUB-NO: JP02000245457A
DOCUMENT-IDENTIFIER: JP 2000245457 A
TITLE: AVERMECTIN AGLYCON SYNTHETASE

PUBN-DATE: September 12, 2000

INVENTOR-INFORMATION:

| NAME | COUNTRY |
|---|---|
| OMURA, SATOSHI | |
| IKEDA, HARUO | |

INT-CL (IPC): C12 N 15/00; A61 K 31/7048; C12 N 1/15; C12 N 9/88; C12 P 19/62; C12 Q 1/68; C07 D 493/22

ABSTRACT:

PROBLEM TO BE SOLVED: To obtain a DNA capable of producing an avermectin-related compound useful as a medicine, a veterinary drug or an agrochemical by encoding avermectin aglycon synthetase.

SOLUTION: This DNA encodes avermectin aglycon synthetase (domain). Furthermore, the DNA has a base sequence selected from a group comprising nucleotide numbers 1-11916 and 11971-30688 of formula I and nucleotide numbers 1-14643 and 14824-31419 of formula II or the DNA encodes a polypeptide hybridized under condition which is stringent to the DNA and having avermection aglycon synthetase activity. The avermectin aglycon synthetase (domain) is obtained by culturing a transformant obtained by introducing a recombinant vector containing the DNA into a host cell which is avermectin producing microbial strain such as Streptomyces avermitilis K 2038 (FERM BP-2775) in a culture medium.

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Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

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☐ 12. Document ID: EP 1160325 A1

L4: Entry 12 of 12 File: EPAB Dec 5, 2001

PUB-NO: EP001160325A1
DOCUMENT-IDENTIFIER: EP 1160325 A1
TITLE: AVERMECTIN AGLYCON SYNTHASE GENES

PUBN-DATE: December 5, 2001

INVENTOR-INFORMATION:

| NAME | COUNTRY |
|---|---|
| OMURA, SATOSHI | JP |
| IKEDA, HARUO | JP |

INT-CL (IPC): C12 N 15/52; C12 N 1/21; C12 N 9/00; C12 N 9/88; C12 P 19/62
EUR-CL (EPC): C12P019/62; C12N015/52

ABSTRACT:

CHG DATE=20020103 STATUS=O> The present invention relates to an isolated DNA which comprises a DNA sequence encoding avermectin aglycon synthase domains that corresponds to multifunctional enzyme proteins involved in the biosynthesis of a polyketide compound, or its mutants having avermectin aglycon synthase activity, particularly functional modules and submodules in the DNA sequence derived from Streptomyces avermitilis, a polypeptide or mutants thereof encoded by the DNA or the mutants, a vector containing the DNA or the mutants, a host cell transformed with the DNA, the mutants thereof, or the vector, and a method for producing avermectin.

**STN SEARCH** **09/914,286** **7/28/03**

```
=> file .nash
=> s avermectin aglycon
L1             3 FILE MEDLINE
L2            39 FILE CAPLUS
L3             8 FILE SCISEARCH
L4             2 FILE LIFESCI
L5             5 FILE BIOSIS
L6             5 FILE EMBASE

TOTAL FOR ALL FILES
L7            62 AVERMECTIN AGLYCON

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8            45 DUP REM L7 (17 DUPLICATES REMOVED)

=> d ab

L8   ANSWER 1 OF 45  CAPLUS  COPYRIGHT 2003 ACS on STN
AB   Genetically engineered Streptomyces avermitilis   ***avermectin***
       ***aglycon***   synthase having domains from polyketide aglycon synthase
     added, and use in and biosynthetic prodn. of 22,23-dihydroavermectin B1a
     and its derivs., are claimed.  The modified enzyme comprises .beta.-keto
     acyl ACP synthase (KS), acyl transferase (AT), dehydrogenase (DH),
     .beta.-keto acyl ACP reductase (KR), and acyl carrier protein (ACP)
     domains plus added enoyl reductase (ER) domain.  Domains from
       ***avermectin***     ***aglycon***   synthase, nemadectin aglycon
     synthase, or milbemycin aglycon synthase, are used.  22,23-
     Dihydroavermectin B1a, which is useful in drugs, veterinary drugs and
     pesticides, can be produced by direct fermn.  Thus, the troublesome and
     difficult industrial steps of purifying avermectin B1a and chem. modifying
     avermectin B1a involved in the conventional are can be omitted and
     therefore 22,23-dihydroavermectin B1a can be industrially produced while
     largely saving the cost and time.  Recombinant expression of modified
       ***avermectin***     ***aglycon***   synthase having DH and KR domains or
     DH, KR, and ACP domains substituted with DH, ER, and KR domains, or DH,
     ER, KR, and ACP domains, from nemadectin aglycon synthase and biosynthetic
     prodn. of 22,23-dihydroavermectin B1a and its derivs., are described.


=> s avermectin
L9           454 FILE MEDLINE
L10         1407 FILE CAPLUS
L11         1124 FILE SCISEARCH
L12          325 FILE LIFESCI
L13         1052 FILE BIOSIS
L14          663 FILE EMBASE

TOTAL FOR ALL FILES
L15         5025 AVERMECTIN

=> s l15 and gene cluster
L16           15 FILE MEDLINE
L17           29 FILE CAPLUS
L18           24 FILE SCISEARCH
L19           12 FILE LIFESCI
L20           15 FILE BIOSIS
L21           18 FILE EMBASE

TOTAL FOR ALL FILES
L22          113 L15 AND GENE CLUSTER

=> s l15 and polyketide synthase
L23           12 FILE MEDLINE
L24           29 FILE CAPLUS
L25           18 FILE SCISEARCH
L26            7 FILE LIFESCI
L27           13 FILE BIOSIS
L28           16 FILE EMBASE
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Entered Medline: 19960826

L44 ANSWER 10 OF 12 MEDLINE on STN
ACCESSION NUMBER: 94280050 MEDLINE
DOCUMENT NUMBER: 94280050 PubMed ID: 8010663
TITLE: Correlation of the ***avermectin*** ***polyketide*** ***synthase*** genes to the ***avermectin*** structure. Implications for designing novel ***avermectins*** .
AUTHOR: MacNeil D J; Occi J L; Gewain K M; MacNeil T
CORPORATE SOURCE: Department of Microbial Chemotherapeutics and Molecular Genetics, Merck Research Laboratories, Merck & Co., Inc., Rahway, New Jersey 07065.
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1994 May 2) 721 123-32.
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940729
Last Updated on STN: 19940729
Entered Medline: 19940719

AB Streptomyces avermitilis produces a series of eight potent anthelmintic compounds called ***avermectins*** (AVM). AVM are pentacyclic, macrocyclic lactone compounds containing an oleandrose disaccharide. Labeling studies have shown that AVM is a polyketide derived from the condensation of 12 acyl units (five propionates and seven acetates) to an isobutyl or 2-methylbutyryl starter unit. The genes required for AVM biosynthesis have been cloned, and deletion mapping has located the AVM gene cluster to a 95-kb region. Partial DNA sequencing of this region indicates two 30-kb segments encode large, multifunctional peptides of the AVM ***polyketide*** ***synthase*** (PKS). The PKS proteins contain at least 49 domains with homology to the domains in fatty acid synthase and erythromycin PKS. These domains are arranged as 12 modular repeats that each encode a PKS unit with various subsets of the FAS-like functions. The predicted functions required to form the side groups on the AVM macrocyclic ring were compared to the functions found in the 12 PKS units. This comparison suggests that each PKS unit is specific for condensation and reduction of one acyl unit. If the various domains can be manipulated without disrupting the PKS, it may be possible to synthesize a variety of AVM derivatives.

L44 ANSWER 11 OF 12 MEDLINE on STN
ACCESSION NUMBER: 92307416 MEDLINE
DOCUMENT NUMBER: 92307416 PubMed ID: 1612425
TITLE: Complex organization of the Streptomyces avermitilis genes encoding the ***avermectin*** ***polyketide*** ***synthase*** .
AUTHOR: MacNeil D J; Occi J L; Gewain K M; MacNeil T; Gibbons P H; Ruby C L; Danis S J
CORPORATE SOURCE: Department of Microbial Chemotherapeutics and Molecular Genetics, Merck Sharp & Dohme Research Laboratories, Rahway, NJ 07065.
SOURCE: GENE, (1992 Jun 15) 115 (1-2) 119-25.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920807
Last Updated on STN: 19970203
Entered Medline: 19920730

AB The ***avermectin*** (Av) ***polyketide*** ***synthase*** (PKS) and erythromycin (Er) PKS are encoded by modular repeats of DNA, but the genetic organization of the modules encoding Av PKS is more complex than Er PKS. Sequencing of several related DNA fragments from Streptomyces avermitilis that are part of the Av biosynthetic gene cluster, revealed that they encode parts of large multifunctional PKS

TOTAL FOR ALL FILES
L29 95 L15 AND POLYKETIDE SYNTHASE

=> s l22 and l29
L30 6 FILE MEDLINE
L31 14 FILE CAPLUS
L32 11 FILE SCISEARCH
L33 4 FILE LIFESCI
L34 5 FILE BIOSIS
L35 8 FILE EMBASE

TOTAL FOR ALL FILES
L36 48 L22 AND L29

=> s l36 not 2001-2003/py
L37 3 FILE MEDLINE
L38 5 FILE CAPLUS
L39 7 FILE SCISEARCH
L40 2 FILE LIFESCI
L41 2 FILE BIOSIS
L42 4 FILE EMBASE

TOTAL FOR ALL FILES
L43 23 L36 NOT 2001-2003/PY

=> dup rem l23
PROCESSING COMPLETED FOR L23
L44 12 DUP REM L23 (0 DUPLICATES REMOVED)

=> d ibib abs 1-12

L44 ANSWER 1 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2002147686 MEDLINE
DOCUMENT NUMBER: 21822493 PubMed ID: 11832500
TITLE: 'Streptomyces nanchangensis', a producer of the insecticidal polyether antibiotic nanchangmycin and the antiparasitic macrolide meilingmycin, contains multiple polyketide gene clusters.
AUTHOR: Sun Yuhui; Zhou Xiufen; Liu Jun; Bao Kai; Zhang Guiming; Tu Guoquan; Kieser Tobias; Deng Zixin
CORPORATE SOURCE: Bio-X Life Science Research Center, Shanghai Jiaotong University, Shanghai 200030, China.
SOURCE: MICROBIOLOGY, (2002 Feb) 148 (Pt 2) 361-71.
Journal code: 9430468. ISSN: 1350-0872.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020308
Last Updated on STN: 20020426
Entered Medline: 20020425

AB Several independent gene clusters containing varying lengths of type I ***polyketide*** ***synthase*** genes were isolated from 'Streptomyces nanchangensis' NS3226, a producer of nanchangmycin and meilingmycin. The former is a polyether compound similar to dianemycin and the latter is a macrolide compound similar to milbemycin, which shares the same macrolide ring as ***avermectin*** but has different side groups. Clusters A-H spanned about 133, 132, 104, 174, 122, 54, 37 and 59 kb, respectively. Two systems were developed for functional analysis of the gene clusters by gene disruption or replacement. (1) Streptomyces phage phiC31 and its derived vectors can infect and lysogenize this strain. (2) pSET152, an Escherichia coli plasmid with phiC31 attP site, and pHZ1358, a Streptomyces-Escherichia coli shuttle cosmid vector, both carrying oriT from RP4, can be mobilized from E. coli into NS3226 by conjugation. pHZ1358 was shown to be generally useful for generating mutant strains by gene disruption and replacement in NS3226 as well as in several other Streptomyces strains. A region in cluster A (approximately 133 kb) seemed to be involved in nanchangmycin production because replacement of several DNA fragments in this region by an apramycin resistance gene [aac3(IV)] gave rise to nanchangmycin non-producing

diversity of the production of the secondary metabolites of Streptomyces. Twenty-five kinds of secondary metabolite gene clusters were found in the genome of S. avermitilis. Four of them are concerned with the biosyntheses of melanin pigments, in which two clusters encode tyrosinase and its cofactor, another two encode an ochronotic pigment derived from homogentiginic acid, and another polyketide-derived melanin. The gene clusters for carotenoid and siderophore biosyntheses are composed of seven and five genes, respectively. There are eight kinds of gene clusters for type-I polyketide compound biosyntheses, and two clusters are involved in the biosyntheses of type-II polyketide-derived compounds. Furthermore, a ***polyketide*** ***synthase*** that resembles phloroglucinol synthase was detected. Eight clusters are involved in the biosyntheses of peptide compounds that are synthesized by nonribosomal peptide synthetases. These secondary metabolite clusters are widely located in the genome but half of them are near both ends of the genome. The total length of these clusters occupies about 6.4% of the genome.

L44 ANSWER 4 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2002054450 MEDLINE
DOCUMENT NUMBER: 21639149 PubMed ID: 11780788
TITLE: Organization of biosynthetic gene cluster for ***avermectin*** in Streptomyces avermitilis: analysis of enzymatic domains in four ***polyketide*** ***synthases*** .
AUTHOR: Ikeda H; Nonomiya T; Omura S
CORPORATE SOURCE: School of Pharmaceutical Sciences, Kitasato University, Tokyo, Japan.
SOURCE: JOURNAL OF INDUSTRIAL MICROBIOLOGY AND BIOTECHNOLOGY, (2001 Sep) 27 (3) 170-6.
Journal code: 9705544. ISSN: 1367-5435.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020511
Entered Medline: 20020510

AB The analysis of the incorporation of 13C-labeled precursors into ***avermectins*** indicates that the ***avermectin*** aglycons are synthesized by head-to-tail condensation of various acyl groups, which is similar to the biosynthesis of other polyketides. ***Polyketide*** ***synthases*** (PKS) use the appropriate CoA ester as a primer and add acetate units from malonyl-CoA and propionate units from methylmalonyl-CoA to assemble the polyketides. ***Avermectin*** aglycons are formed by addition to the starter unit (2-methylbutyrate or isobutyrate) of 12 acyl condensations in the order P-A-A-A-A-P-P-A-P-A-P-A (P, propionyl; A, acetyl). Within the 90-kb gene cluster for a vermectin biosynthesis, the central 65-kb segment was found to be required for aglycon biosynthesis by phenotypic analysis of strains containing deletion or insertion mutations in this region. A complete sequence analysis of the 65-kb segment indicated that this segment encodes ***avermectin*** PKS. The ***avermectin*** PKS genes are organized into two converging blocks of ORFs. From the results of sequencing analysis, a feature of the two regions, aveA1/aveA2 and avea3/aveA4, is that they encode four kinds of large multifunctional polypeptides containing 55 domains which possess putative fatty acid synthase-like activities. The ***avermectin*** PKS (AVES 1-4) appear to contain two, three, or four modules. AVES1 and 2 contain two and four modules, respectively, whereas AVES 3 and AVES 4 each contains three modules. The 12 modules correspond to the 12 cycles required for synthesis of the ***avermectin*** aglycon.

L44 ANSWER 5 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2001317418 MEDLINE
DOCUMENT NUMBER: 21285058 PubMed ID: 11392681
TITLE: Genetic analysis of biosynthesis of polyketide compound in Streptomyces avermitilis.
AUTHOR: Ikeda H
SOURCE: JAPANESE JOURNAL OF ANTIBIOTICS, (2001 Mar) 54 (3) 112-6.
Journal code: 0154402. ISSN: 0368-2781.
PUB. COUNTRY: Japan

DOCUMENT TYPE: (LECTURES)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726

L44 ANSWER 6 OF 12 MEDLINE on STN
ACCESSION NUMBER: 1999380548 MEDLINE
DOCUMENT NUMBER: 99380548 PubMed ID: 10449723
TITLE: Organization of the biosynthetic gene cluster for the polyketide anthelmintic macrolide ***avermectin*** in Streptomyces avermitilis.
AUTHOR: Ikeda H; Nonomiya T; Usami M; Ohta T; Omura S
CORPORATE SOURCE: School of Pharmaceutical Sciences, Kitasato University, Tokyo 108-8641, Japan.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Aug 17) 96 (17) 9509-14. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB032367; GENBANK-AB032523; GENBANK-AB032524
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990909

AB Analysis of the gene cluster from Streptomyces avermitilis that governs the biosynthesis of the polyketide anthelmintic ***avermectin*** revealed that it contains four large ORFs encoding giant multifunctional polypeptides of the ***avermectin*** ***polyketide*** ***synthase*** (AVES 1, AVES 2, AVES 3, and AVES 4). These clustered ***polyketide*** ***synthase*** genes responsible for ***avermectin*** biosynthesis together encode 12 homologous sets of enzyme activities (modules), each catalyzing a specific round of polyketide chain elongation. The clustered genes encoding ***polyketide*** ***synthase*** are organized as two sets of six modular repeats, aveA1-aveA2 and aveA3-aveA4, which are convergently transcribed. The total of 55 constituent active sites makes this the most complex multifunctional enzyme system identified to date. The sequenced DNA region contains 14 additional ORFs, some of which encode polypeptides governing other key steps in ***avermectin*** biosynthesis. Between the two sets of ***polyketide*** ***synthase*** genes lie two genes involved in postpolyketide modification, one of which encodes cynthochrome P450 hydroxylase that probably catalyzes furan ring formation at C6 to C8a. Immediately right of the large ***polyketide*** ***synthase*** genes is a set of genes involved in oleandrose biosynthesis and its transglycosylation to polyketide-derived aglycons. This cluster includes nine genes, but one is not functional in the biosynthesis of ***avermectin*** . On the left side of ***polyketide*** ***synthase*** genes, two ORFs encoding methyltransferase and nonpolyketide synthase ketoreductase involved in postpolyketide modification are located to the left of the ***polyketide*** ***synthase*** genes, and an adjacent gene encodes a regulatory function that may be involved in activation of the transcription of ***avermectin*** biosynthetic genes.

L44 ANSWER 7 OF 12 MEDLINE on STN
ACCESSION NUMBER: 1999114955 MEDLINE
DOCUMENT NUMBER: 99114955 PubMed ID: 9918396
TITLE: Novel erythromycins from a recombinant Saccharopolyspora erythraea strain NRRL 2338 pIG1. I. Fermentation, isolation and biological activity.
AUTHOR: Pacey M S; Dirlam J P; Geldart R W; Leadlay P F; McArthur H A; McCormick E L; Monday R A; O'Connell T N; Staunton J; Winchester T J
CORPORATE SOURCE: Animal Health Central Research, Pfizer Central Research, Sandwich, Kent, UK.
SOURCE: JOURNAL OF ANTIBIOTICS, (1998 Nov) 51 (11) 1029-34.

Journal code: 0151115. ISSN: 0021-8820.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 19990223
Entered Medline: 19990209

AB In a previous report, a plasmid, pIG1, which contained the loading domain from the Streptomyces avermitilis ***polyketide*** ***synthase*** (PKS), promoters from Streptomyces coelicolor and the DEBS1-TE truncated PKS from Saccharopolyspora erythraea, was integrated into the S. erythraea chromosome, effectively replacing the natural erythromycin loading domain with the ***avermectin*** loading domain. In this paper, we report the feeding of short-chained fatty acids to this recombinant strain, and its parent, NRRL 2338. Both strains incorporated exogenously supplied fatty acids to produce novel, biologically active, C-13 substituted erythromycins.

L44 ANSWER 8 OF 12 MEDLINE on STN
ACCESSION NUMBER: 1998084717 MEDLINE
DOCUMENT NUMBER: 98084717 PubMed ID: 9422686
TITLE: Engineering broader specificity into an antibiotic-producing ***polyketide*** ***synthase***
.
AUTHOR: Marsden A F; Wilkinson B; Cortes J; Dunster N J; Staunton J; Leadlay P F
CORPORATE SOURCE: Cambridge Centre for Molecular Recognition and Department of Biochemistry, University of Cambridge, Tennis Court Road, Cambridge, CB2 1QW, UK.
SOURCE: SCIENCE, (1998 Jan 9) 279 (5348) 199-202.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980129

AB The wide-specificity loading module for the ***avermectin*** -producing ***polyketide*** ***synthase*** was grafted onto the first multienzyme component (DEBS1) of the erythromycin-producing ***polyketide*** ***synthase*** in place of the normal loading module. Expression of this hybrid enzyme in the erythromycin producer Saccharopolyspora erythraea produced several novel antibiotic erythromycins derived from endogenous branched-chain acid starter units typical of natural ***avermectins*** . Because the ***avermectin*** ***polyketide*** ***synthase*** is known to accept more than 40 alternative carboxylic acids as starter units, this approach opens the way to facile production of novel analogs of antibiotic macrolides.

L44 ANSWER 9 OF 12 MEDLINE on STN
ACCESSION NUMBER: 96271257 MEDLINE
DOCUMENT NUMBER: 96271257 PubMed ID: 8688633
TITLE: ***Avermectins*** .
AUTHOR: MacNeil D J
CORPORATE SOURCE: Department of Molecular Phamacology & Biochemistry, Merck Laboratory, Rahway NJ 07065, USA.
SOURCE: BIOTECHNOLOGY, (1995) 28 421-42. Ref: 59
Journal code: 8300602. ISSN: 0740-7378.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960911
Last Updated on STN: 19960911

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L15        5025 S AVERMECTIN
L16          15 FILE MEDLINE
L17          29 FILE CAPLUS
L18          24 FILE SCISEARCH
L19          12 FILE LIFESCI
L20          15 FILE BIOSIS
L21          18 FILE EMBASE
     TOTAL FOR ALL FILES
L22         113 S L15 AND GENE CLUSTER
L23          12 FILE MEDLINE
L24          29 FILE CAPLUS
L25          18 FILE SCISEARCH
L26           7 FILE LIFESCI
L27          13 FILE BIOSIS
L28          16 FILE EMBASE
     TOTAL FOR ALL FILES
L29          95 S L15 AND POLYKETIDE SYNTHASE
L30           6 FILE MEDLINE
L31          14 FILE CAPLUS
L32          11 FILE SCISEARCH
L33           4 FILE LIFESCI
L34           5 FILE BIOSIS
L35           8 FILE EMBASE
     TOTAL FOR ALL FILES
L36          48 S L22 AND L29
L37           3 FILE MEDLINE
L38           5 FILE CAPLUS
L39           7 FILE SCISEARCH
L40           2 FILE LIFESCI
L41           2 FILE BIOSIS
L42           4 FILE EMBASE
     TOTAL FOR ALL FILES
L43          23 S L36 NOT 2001-2003/PY
L44          12 DUP REM L23 (0 DUPLICATES REMOVED)

=> s l7 not 2001-2002/py
L45           2 FILE MEDLINE
L46          32 FILE CAPLUS
L47           7 FILE SCISEARCH
L48           1 FILE LIFESCI
L49           4 FILE BIOSIS
L50           4 FILE EMBASE

TOTAL FOR ALL FILES
L51          50 L7 NOT 2001-2002/PY

=> dup rem l51
PROCESSING COMPLETED FOR L51
L52          38 DUP REM L51 (12 DUPLICATES REMOVED)

=> d 1-38 ibib abs

L52  ANSWER 1 OF 38  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:87073  CAPLUS
DOCUMENT NUMBER:          138:148678
TITLE:                    Domain swapping of   ***avermectin***
                            ***aglycon***   synthase for avermectin B1a
                          biosynthesis
INVENTOR(S):              Omura, Satoru; Ikeda, Haruo; Endo, Hirofumi
PATENT ASSIGNEE(S):       Kyowa Hakko Kogyo Co., Ltd., Japan; Kitasato Institute
SOURCE:                   Jpn. Kokai Tokkyo Koho, 266 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     JP 2003033188      A2   20030204       JP 2001-318232   20011016
PRIORITY APPLN. INFO.:                   JP 2001-142941   A  20010514
```

AB Genetically engineered Streptomyces avermitilis ***avermectin*** ***aglycon*** synthase having domains from polyketide aglycon synthase added, and use in and biosynthetic prodn. of 22,23-dihydroavermectin B1a and its derivs., are claimed. The modified enzyme comprises .beta.-keto acyl ACP synthase (KS), acyl transferase (AT), dehydrogenase (DH), .beta.-keto acyl ACP reductase (KR), and acyl carrier protein (ACP) domains plus added enoyl reductase (ER) domain. Domains from ***avermectin*** ***aglycon*** synthase, nemadectin aglycon synthase, or milbemycin aglycon synthase, are used. 22,23-Dihydroavermectin B1a, which is useful in drugs, veterinary drugs and pesticides, can be produced by direct fermn. Thus, the troublesome and difficult industrial steps of purifying avermectin B1a and chem. modifying avermectin B1a involved in the conventional are can be omitted and therefore 22,23-dihydroavermectin B1a can be industrially produced while largely saving the cost and time. Recombinant expression of modified ***avermectin*** ***aglycon*** synthase having DH and KR domains or DH, KR, and ACP domains substituted with DH, ER, and KR domains, or DH, ER, KR, and ACP domains, from nemadectin aglycon synthase and biosynthetic prodn. of 22,23-dihydroavermectin B1a and its derivs., are described.

L52 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:176271 CAPLUS
DOCUMENT NUMBER: 130:324974
TITLE: Methoxymethylation of Alcohols, Phenols, and ***Avermectin*** ***Aglycons*** Using MOM 2-pyridyl sulfide
AUTHOR(S): Marcune, Benjamin F.; Karady, Sandor; Dolling, Ulf-H.; Novak, Thomas J.
CORPORATE SOURCE: Department of Process Research Merck Research Laboratories, Merck Co., Rahway, NJ, 07065, USA
SOURCE: Journal of Organic Chemistry (1999), 64(7), 2446-2449
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:324974
AB Methoxymethyl 2-pyridyl sulfide (MOM-ON) is an effective methoxymethylating reagent when used in conjunction with AgOTf, NaOAc, and THF. A wide range of MOM ethers are produced from phenols and alcs., including tertiary and allylic alcs., in good yields and under mild, neutral conditions. This method is also effective for the methoxymethylation of ***avermectin*** ***aglycons*** .
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:726147 CAPLUS
DOCUMENT NUMBER: 132:63188
TITLE: Screening of spontaneous and induced mutants in Streptomyces avermitilis enhances avermectin production
AUTHOR(S): Aikawa, M.; Lopes-Shikida, S. A. R.; Lemos, M. F.; Pradella, J. G. C.; Padilla, G.
CORPORATE SOURCE: Instituto de Ciencias Biomedicas, Departamento de Microbiologia, Universidade de Sao Paulo, Sao Paulo, CEP 05508-900, Brazil
SOURCE: Applied Microbiology and Biotechnology (1999), 52(4), 558-562
CODEN: AMBIDG; ISSN: 0175-7598
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Because of the loss of productivity in industrial strains (as a consequence of genetic instability), the selection of spontaneous and induced mutants in Streptomyces might generate enhanced producers of bioactive compds. In this work, a spontaneously high producing mutant of S. avermitilis, strain 267/2H, was isolated. This mutant produced 8.2-fold more avermectin B1 than the wild type and it was treated with Me methanesulfonate (MMS) in order to obtain better avermectin producers. One mutant, strain IPT-85, produced about 16 times more avermectin than the wild-type strain ATCC 31267 and twice as much as the parental strain

proteins. The Av PKS proteins show strong similarity to each other, as well as similarity to Er PKS proteins [Donadio et al., Science 252 (1991) 675-679] and fatty acid synthases. Partial DNA sequencing of the 65-kb region containing all the related sequence elements in the avr genes provides evidence for twelve modular repeats encoding FAS-like domains. The genes encoding the Av PKS are organized as two sets of six modular repeats which are convergently transcribed.

L44 ANSWER 12 OF 12 MEDLINE on STN
ACCESSION NUMBER: 87144590 MEDLINE
DOCUMENT NUMBER: 87144590 PubMed ID: 3029594
TITLE: Homology between Streptomyces genes coding for synthesis of different polyketides used to clone antibiotic biosynthetic genes.
AUTHOR: Malpartida F; Hallam S E; Kieser H M; Motamedi H; Hutchinson C R; Butler M J; Sugden D A; Warren M; McKillop C; Bailey C R; +
CONTRACT NUMBER: CA35381 (NCI)
SOURCE: NATURE, (1987 Feb 26-Mar 4) 325 (6107) 818-21. Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198704
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870408

AB Many important antibiotics such as tetracyclines, erythromycin, adriamycin, monensin, rifamycin and ***avermectins*** are polyketides. In their biosynthesis, multifunctional synthases catalyse iterated condensation of thio-esters derived from acetate, propionate or butyrate to yield aliphatic chains of varying length and carrying different alkyl substituents. Subsequent modifications, including aromatic or macrolide ring closure or specific methylations or glycosylations, generate further chemical diversity. It has been suggested that, if different ***polyketide*** ***synthases*** had a common evolutionary origin, cloned DNA coding for one synthase might be used as a hybridization probe for the isolation of others. We show here that this is indeed possible. Study of a range of such synthase genes and their products should help to elucidate what determines the choice and order of condensation of different residues in polyketide assembly, and might yield, by in vitro recombination or mutagenesis, synthase genes capable of producing novel antibiotics. Moreover, because genes for entire antibiotic pathways are usually clustered in Streptomyces, cloned ***polyketide*** ***synthase*** genes are valuable in giving access to groups of linked biosynthetic genes.

=> d his

(FILE 'HOME' ENTERED AT 17:10:27 ON 28 JUL 2003)

FILE 'MEDLINE, CAPLUS, SCISEARCH, LIFESCI, BIOSIS, EMBASE' ENTERED AT 17:11:08 ON 28 JUL 2003

| | | |
|---|---|---|
| L1 | 3 | FILE MEDLINE |
| L2 | 39 | FILE CAPLUS |
| L3 | 8 | FILE SCISEARCH |
| L4 | 2 | FILE LIFESCI |
| L5 | 5 | FILE BIOSIS |
| L6 | 5 | FILE EMBASE |
| | | TOTAL FOR ALL FILES |
| L7 | 62 | S AVERMECTIN AGLYCON |
| L8 | 45 | DUP REM L7 (17 DUPLICATES REMOVED) |
| L9 | 454 | FILE MEDLINE |
| L10 | 1407 | FILE CAPLUS |
| L11 | 1124 | FILE SCISEARCH |
| L12 | 325 | FILE LIFESCI |
| L13 | 1052 | FILE BIOSIS |
| L14 | 663 | FILE EMBASE |
| | | TOTAL FOR ALL FILES |

TITLE: Avermectins and milbemycins
AUTHOR(S): Davies, H. G.; Green, R. H.
CORPORATE SOURCE: Med. Chem. Dep., Glaxo Group Res., Greenford, UB6 0HE, UK
SOURCE: Natural Product Reports (1986), 3(2), 87-121
CODEN: NPRRDF; ISSN: 0265-0568
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 104 refs. including fermn. and isolation, structure detn., biosynthesis, metab., syntheses, chem. interconversions, protection and acylation, oxidns., alkylation, redn., ***avermectin*** ***aglycons*** and their monosaccharide analogs, and structure-activity relationships.

L52 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:478763 CAPLUS
DOCUMENT NUMBER: 105:78763
TITLE: Avermectin and milbemycin 13-keto, 13-imino and 13-amino derivatives
INVENTOR(S): Linn, Bruce O.; Mrozik, Helmut H.
PATENT ASSIGNEE(S): Merck and Co., Inc. , USA
SOURCE: Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 165029 | A1 | 19851218 | EP 1985-304063 | 19850607 |
| EP 165029 | B1 | 19891102 | | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| US 4579864 | A | 19860401 | US 1984-619238 | 19840611 |
| AU 8543409 | A1 | 19851219 | AU 1985-43409 | 19850607 |
| AU 569624 | B2 | 19880211 | | |
| ZA 8504364 | A | 19860226 | ZA 1985-4364 | 19850610 |
| JP 61022087 | A2 | 19860130 | JP 1985-125281 | 19850611 |
| JP 07053734 | B4 | 19950607 | | |

PRIORITY APPLN. INFO.: US 1984-619238 19840611
GI

/ Structure 15 in file .gra /

AB The aglycon title compds. I (broken line = single or double bond; R1 = H, OH, C1-5 alkanoyloxy or O, provided that R1 is present only when broken line indicates single bond; R2 = C1-4 alkyl; R3 = OH, C1-5 alkoxy, -alkanoyloxy; R4 = H, OH, pyridinylcarbonyloxy; Y = O, NH2, NOH, etc.) and their trisubstituted silyl-protected derivs., useful as insecticides and parasiticides (no data) were prepd. Thus, avermectin A2a/A2b aglycon was silylated to give 23-O-tert-butyldimethylsilyl derivs., and desilylated to give 13-oxoavermectin A2a/A2b aglycon.

L52 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:65474 CAPLUS
DOCUMENT NUMBER: 104:65474
TITLE: Demethylavermectins. Biosynthesis, isolation and characterization
AUTHOR(S): Schulman, Marvin D.; Valentino, Delia; Hensens, Otto D.; Zink, Deborah; Nallin, Mary; Kaplan, L.; Ostlind, D. A.
CORPORATE SOURCE: Dep. Ferment. Microbiol., Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07075, USA
SOURCE: Journal of Antibiotics (1985), 38(11), 1494-8
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Streptomyces avermitilis Normally produces 8 avermectins. Avermectin A components contain 3 methoxyl groups: 2 on the oleandrose disaccharide and

1 on the aglycon moiety at C5. Avermectin B components contain methoxyl groups only on the oleandrose disaccharide. Sinefungin inhibits methylation at all 3 sites. Addn. of sinefungin to S. avermitilis Agly-1, a mutant which produces virtually only ***avermectin*** ***aglycon*** A components, alters the fermn. and causes an accumulation of ***avermectin*** ***aglycon*** B components. Addn. of sinefungin to S. avermitilis 08, a high-producing strain, results in accumulation of 8 new avermectins which lack methoxyl groups on the oleandrose moieties as well as on the aglycon. These new avermectins were isolated and shown to possess anthelmintic and insecticidal activity.

L52 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:120737 CAPLUS
DOCUMENT NUMBER: 100:120737
TITLE: Synthesis of milbemycins from avermectins
AUTHOR(S): Mrozik, H.; Chabala, J. C.; Eskola, P.; Matzuk, A.; Waksmunski, F.; Woods, M.; Fisher, M. H.
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Tetrahedron Letters (1983), 24(48), 5333-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

/ Structure 16 in file .gra /

AB The structures of the avermectins and the milbemycins were iterrelated by the conversion of 22,23-dihydroavermectin B1a and B1b aglycons (I, R = Et, Me, R1 = OH) into 13-deoxy-22,23-dihydroavermectin B1a aglycon (I, R = Et, R1 = H) and 13-deoxy-22,23-dihydroavermectin B1b aglycon (I, R = Me, R1 = H), corresponding to 26-ethylmilbemycin-.alpha.3 and milbemycin B-41D resp., via redn. of the protected 13-chloroaglycone derivs.

L52 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1982:52597 CAPLUS
DOCUMENT NUMBER: 96:52597
TITLE: ***Avermectin*** ***aglycons***
AUTHOR(S): Mrozik, Helmut; Eskola, Philip; Arison, Byron H.; Albers-Schoenberg, George; Fisher, Michael H.
CORPORATE SOURCE: Merck Sharp & Dohme Res. Lab., Rahway, NJ, USA
SOURCE: Journal of Organic Chemistry (1982), 47(3), 489-92
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reaction of avermectin A2a and B2a with MeOH-1% concd. H2SO4 gave the aglycons; alcoholysis in Me2CHOH-1% concd. H2SO4 gave the monosaccharides. Acid-catalyzed methanolysis of avermectin B1a (I), however, gave a mixt. of 3 compds. identified as the aglycon and the 2 epimeric 22,23-dihydro-23-O-methoxyaglycons formed by addn. of MeOH to the 22,23 double bond of I. The structures were detd. by 1H and 13C NMR and mass spectra. Hydrolysis of I in aq. tetrahydrofuran-10% concd. H2SO4 gave a mixt. of monosaccharide and aglycon.

L52 ANSWER 38 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 82:49616 SCISEARCH
THE GENUINE ARTICLE: MZ709
TITLE: ***AVERMECTIN*** ***AGLYCONS***
AUTHOR: MROZIK H (Reprint); ESKOLA P; ARISON B H; ALBERSSCHONBERG G; FISHER M H
CORPORATE SOURCE: MERCK SHARP & DOHME, RES LABS, RAHWAY, NJ, 07065 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (1982) Vol. 47, No. 3, pp. 489-492.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 13

mutants.

L44 ANSWER 2 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2002170852 MEDLINE
DOCUMENT NUMBER: 21899102 PubMed ID: 11902441
TITLE: Biosynthesis and attachment of novel bacterial ***polyketide*** ***synthase*** starter units.
AUTHOR: Moore Bradley S; Hertweck Christian
CORPORATE SOURCE: Division of Medicinal Chemistry, College of Pharmacy, University of Arizona, Tucson 85721-0207, USA.. moore@pharmacy.arizona.edu
CONTRACT NUMBER: AI47818 (NIAID)
SOURCE: NATURAL PRODUCT REPORTS, (2002 Feb) 19 (1) 70-99. Ref: 240
Journal code: 8502408. ISSN: 0265-0568.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020321
Last Updated on STN: 20020514
Entered Medline: 20020513

AB The biosynthesis and mode of attachment of a wide range of ***polyketide*** ***synthase*** (PKS) starter units in bacteria are covered in this review. Natural, unnatural, and engineered starter units associated with type I and type II PKSs are reported. The literature through early 2001 is reviewed, and 240 references cited.

L44 ANSWER 3 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2001559212 MEDLINE
DOCUMENT NUMBER: 21477403 PubMed ID: 11572948
TITLE: Genome sequence of an industrial microorganism Streptomyces avermitilis: deducing the ability of producing secondary metabolites.
AUTHOR: Omura S; Ikeda H; Ishikawa J; Hanamoto A; Takahashi C; Shinose M; Takahashi Y; Horikawa H; Nakazawa H; Osonoe T; Kikuchi H; Shiba T; Sakaki Y; Hattori M
CORPORATE SOURCE: The Kitasato Institute for Life Sciences, Kitasato University, Tokyo 108-8642, Japan.. omura-s@kitasato.or.jp
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Oct 9) 98 (21) 12215-20.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB070934; GENBANK-AB070935; GENBANK-AB070936; GENBANK-AB070937; GENBANK-AB070938; GENBANK-AB070939; GENBANK-AB070940; GENBANK-AB070941; GENBANK-AB070942; GENBANK-AB070943; GENBANK-AB070944; GENBANK-AB070945; GENBANK-AB070946; GENBANK-AB070947; GENBANK-AB070948; GENBANK-AB070949; GENBANK-AB070950; GENBANK-AB070951; GENBANK-AB070952; GENBANK-AB070953; GENBANK-AB070954; GENBANK-AB070955; GENBANK-AB070956; GENBANK-AB070957
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011022
Last Updated on STN: 20030105
Entered Medline: 20011228

AB Streptomyces avermitilis is a soil bacterium that carries out not only a complex morphological differentiation but also the production of secondary metabolites, one of which, ***avermectin*** , is commercially important in human and veterinary medicine. The major interest in this genus Streptomyces is the diversity of its production of secondary metabolites as an industrial microorganism. A major factor in its prominence as a producer of the variety of secondary metabolites is its possession of several metabolic pathways for biosynthesis. Here we report sequence analysis of S. avermitilis, covering 99% of its genome. At least 8.7 million base pairs exist in the linear chromosome; this is the largest bacterial genome sequence, and it provides insights into the intrinsic

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TOTAL FOR ALL FILES
L29         95 L15 AND POLYKETIDE SYNTHASE

=> s l22 and l29
L30          6 FILE MEDLINE
L31         14 FILE CAPLUS
L32         11 FILE SCISEARCH
L33          4 FILE LIFESCI
L34          5 FILE BIOSIS
L35          8 FILE EMBASE

TOTAL FOR ALL FILES
L36         48 L22 AND L29

=> s l36 not 2001-2003/py
L37          3 FILE MEDLINE
L38          5 FILE CAPLUS
L39          7 FILE SCISEARCH
L40          2 FILE LIFESCI
L41          2 FILE BIOSIS
L42          4 FILE EMBASE

TOTAL FOR ALL FILES
L43         23 L36 NOT 2001-2003/PY

=> dup rem l23
PROCESSING COMPLETED FOR L23
L44          12 DUP REM L23 (0 DUPLICATES REMOVED)

=> d ibib abs 1-12

L44  ANSWER 1 OF 12     MEDLINE on STN
ACCESSION NUMBER:   2002147686     MEDLINE
DOCUMENT NUMBER:    21822493   PubMed ID: 11832500
TITLE:              'Streptomyces nanchangensis', a producer of the
                    insecticidal polyether antibiotic nanchangmycin and the
                    antiparasitic macrolide meilingmycin, contains multiple
                    polyketide gene clusters.
AUTHOR:             Sun Yuhui; Zhou Xiufen; Liu Jun; Bao Kai; Zhang Guiming; Tu
                    Guoquan; Kieser Tobias; Deng Zixin
CORPORATE SOURCE:   Bio-X Life Science Research Center, Shanghai Jiaotong
                    University, Shanghai 200030, China.
SOURCE:             MICROBIOLOGY, (2002 Feb) 148 (Pt 2) 361-71.
                    Journal code: 9430468. ISSN: 1350-0872.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200204
ENTRY DATE:         Entered STN: 20020308
                    Last Updated on STN: 20020426
                    Entered Medline: 20020425
AB   Several independent gene clusters containing varying lengths of type I
       ***polyketide***     ***synthase***   genes were isolated from
     'Streptomyces nanchangensis' NS3226, a producer of nanchangmycin and
     meilingmycin.  The former is a polyether compound similar to dianemycin
     and the latter is a macrolide compound similar to milbemycin, which shares
     the same macrolide ring as   ***avermectin***   but has different side
     groups.  Clusters A-H spanned about 133, 132, 104, 174, 122, 54, 37 and 59
     kb, respectively.  Two systems were developed for functional analysis of
     the gene clusters by gene disruption or replacement. (1) Streptomyces
     phage phiC31 and its derived vectors can infect and lysogenize this
     strain. (2) pSET152, an Escherichia coli plasmid with phiC31 attP site,
     and pHZ1358, a Streptomyces-Escherichia coli shuttle cosmid vector, both
     carrying oriT from RP4, can be mobilized from E. coli into NS3226 by
     conjugation. pHZ1358 was shown to be generally useful for generating
     mutant strains by gene disruption and replacement in NS3226 as well as in
     several other Streptomyces strains.  A region in cluster A (approximately
     133 kb) seemed to be involved in nanchangmycin production because
     replacement of several DNA fragments in this region by an apramycin
     resistance gene [aac3(IV)] gave rise to nanchangmycin non-producing
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267/2H. Reversion studies showed that avermectin prodn. by the IPT-85 mutant was unstable and required const. selection to maintain high levels of avermectin B1 prodn. Upon a 2nd MMS treatment of IPT-85, a new ***avermectin*** ***aglycon*** -producing mutant, strain IPT 85-62, was isolated.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:285351 CAPLUS
DOCUMENT NUMBER: 131:84366
TITLE: Genetic analysis of polyketide synthesis in avermectin biosynthesis
AUTHOR(S): Ikeda, Haruo; Nonomiya, Tomoko; Omura, Satoshi
CORPORATE SOURCE: School of Pharmaceutical Sciences, Kitasato University, Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1998), 40th, 19-24
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 6 refs. The proposed avermectin biosynthesis pathway is based on evidence obtained from several studies, including incorporation of labeled precursors into the avermectins and identification of key intermediates produced by biosynthetically blocked mutants or wild type-producing strains. The results of the incorporation of 13C-labeled precursors and anal. of the resulting 13C-labeled avermectin indicate that the ***avermectin*** ***aglycons*** are derived by head-to-tail condensation of various acyl groups which is similar to the biosynthesis of the other polyketides. The polyketide synthases use the appropriate CoA ester as a primer and add acetate units from malonyl-CoA and propionate units from methylmalonyl-CoA to assemble the polyketides. ***Avermectin*** ***aglycon*** is formed by addn. of the starter unit (2-methylbutyrate or isobutyrate), of 12 acyl condensations in the order P-A-A-A-A-P-P-A-P-A-P-A (P, propionyl; A, acetyl). Within the 95 kbp gene cluster for avermectin biosynthesis, the central 65 kbp segment was found to be required for aglycon biosynthesis by phenotypic anal. of strains contg. deletion or insertion mutations in this region. A sequence anal. of the central 65 kbp segment within the gene cluster for avermectin biosynthesis indicated that this segment encodes avermectin polyketide synthases. The avermectin polyketide synthase genes are organized into two converging blocks of ORFs. From the results of sequencing anal., a feature of the two regions, aveAI and aveAII, is that they encode four kinds of large multifunctional polypeptides contains domains possessing putative fatty acid synthase-like activities. The PKS genes for avermectin biosynthesis are organized into two convergently transcribed clusters of six modules. The avermectin PKS proteins appear to contain two, three, or four synthase units (SU). PKS-1 with two SUs and PKS-2 with four SUs contain modules 1 and 2, and 3-6, resp., whereas PKS-3 and -4 with three SUs contain modules 7-9, and modules 10-12, resp. The 12 SUs correspond to the 12 cycles required for synthesis of the initial aglycon.

L52 ANSWER 5 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 97:463097 SCISEARCH
THE GENUINE ARTICLE: XE015
TITLE: Practical syntheses of 13-O-[(2-methoxyethoxy)methyl]-22,23-dihydroavermectin B-1 aglycon [dimedectin isopropanol, MK-324] and 13-epi-O-(methoxymethyl)-22,23-dihydroavermectin B-1 aglycon [L-694,554], flea active ivermectin analogues
AUTHOR: Cvetovich R J (Reprint); Senanayake C H; Amato J S; DiMichele L M; Bill T J; Larsen R D; Shuman R F; Verhoeven T R; Grabowski E J J
CORPORATE SOURCE: MERCK RES LABS, DEPT PROC RES, POB 2000, RAHWAY, NJ 07065 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (13 JUN 1997) Vol. 62, No. 12, pp. 3989-3993.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW,

WASHINGTON, DC 20036.
ISSN: 0022-3263.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 19
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Practical high yielding syntheses of 13-O-[(2-methoxyethoxy)methyl]-22,23-dihydroavermectin B-1 aglycon (dimedectin 2-propanol, MK-324, 1) and 13-epi-O-(methoxymethyl)-22,23-dihydroavermectin B-1 aglycon (L-694,554, 2), both potent flea insecticides, from ivermectin are presented. The successful selective manipulation of silyl protecting groups on ivermectin aglycon led to the facile preparation of 5,7-O-bis-silyl-22,23-dihydroavermectin B-1 aglycon 7 as the key intermediate for the large scale syntheses of these compounds. Development of a dual pyridine/tertiary amine system for mesylation of the C-13 alpha hydroxyl group of 7 and subsequent displacement with cesium propionate-propionic acid led to the successful inversion of the 13-hydroxy group.

L52 ANSWER 6 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 97:195778 SCISEARCH
THE GENUINE ARTICLE: WL042
TITLE: Synthesis of 5-deoxy-5-oxomilbemycin A(4) 5-hydrazone derivatives and their activity against Tetranychus urticae
AUTHOR: Tsukamoto Y (Reprint); Sato K; Tanaka K; Yanai T
CORPORATE SOURCE: SANKYO CO LTD, AGROSCI RES LABS, 1041 YASU, YASO, SHIGA 52023, JAPAN (Reprint)
COUNTRY OF AUTHOR: JAPAN
SOURCE: BIOSCIENCE BIOTECHNOLOGY AND BIOCHEMISTRY, (FEB 1997) Vol. 61, No. 2, pp. 304-311.
Publisher: JAPAN SOC BIOSCI BIOTECHN AGROCHEM, JAPAN ACAD SOC CTR BLDG, 2-4-6 YAYOI BUNKYO-KU, TOKYO 113, JAPAN.
ISSN: 0916-8451.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: English
REFERENCE COUNT: 41
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB 5-Deoxy-5-oxomilbemycin A(4) 5-hydrazone derivatives were synthesized by a condensation reaction of 5-deoxy-5-oxomilbemycin A(4) (2) with hydrazines. Acetic acid played an important role to give each hydrazone in a good yield by regulating the reactivity of ketone 2 and the hydrazines. The acaricidal activity of each synthesized compound was studied on the primary leaves of plants of the Vigna sinensis Savi species infected with organic phosphate-sensitive mites (Tetranychus urticae), Some of the synthesized derivatives exhibited higher miticidal activity than that of milbemycin A(4). Among them, 5-deoxy-5-oxomilbemycin A(4) 5-N-(N',N'-dimethylcarbamoyl)hydrazone (18) totally controlled the mites at a concentration of 3 ppm.

L52 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:662513 CAPLUS
DOCUMENT NUMBER: 123:54274
TITLE: Bioconversion products of 27-hydroxy avermectin
INVENTOR(S): Arison, Byron H.; Doherty, Patrick J.; Schulman, Marvin D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Brit. UK Pat. Appl., 45 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 2281911 | A1 | 19950322 | GB 1994-18478 | 19940914 |
| US 5478929 | A | 19951226 | US 1994-247173 | 19940520 |
| PRIORITY APPLN. INFO.: | | | US 1993-123181 | 19930915 |

GI

/ Structure 1 in file .gra /

AB Both isomers of 27-hydroxyavermectin aglycons represented by compd. (I) wherein the broken line at the 22,23-position indicates a single or double bond, R1 is present only when the broken line is a single bond, R1 is H, and the wavy line at the 27-position represents the A and B isomers, are produced by cultivating a strain of Saccharopolyspora erythraea in a nutrient medium contg. assimilable sources of N and C and an ***avermectin*** ***aglycon*** substrate under aerobic conditions until a substantial amt. of I is produced and isolating the I so produced. I may be converted to other avermectin derivs., e.g. 4''-O-glucosyl-27-hydroxyivermectin and 4''-O-glucosyl-27-hydroxyavermectin B1a.

L52 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:30611 CAPLUS
DOCUMENT NUMBER: 120:30611
TITLE: Process for inverting the 13-(alpha)-hydroxy group of ***avermectin*** ***aglycons***
INVENTOR(S): Bill, Timothy; Senanayake, Chris H.; Larsen, Robert D.; Singh, Sheo B.; Vernhoeven, Thomas R.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5241083 | A | 19930831 | US 1992-907429 | 19920701 |

PRIORITY APPLN. INFO.: US 1992-907429 19920701
OTHER SOURCE(S): CASREACT 120:30611; MARPAT 120:30611
AB The natural stereochem. at the 13 position of ***avermectin*** ***aglycons*** , normally .alpha.-oriented or below the plane of the mol., is inverted or epimerized into the .beta. position. This procedure starts with the ***avermectin*** ***aglycon*** compds. where the 13 .alpha.-hydroxy group is activated into a mesylate leaving group which is displaced with a Cs carboxylate and one equiv. of the resp. carboxylic acid, ending with ester group being converted to the 13-.beta. hydroxy configuration by transesterification and in high yield.

L52 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:167616 CAPLUS
DOCUMENT NUMBER: 118:167616
TITLE: Microbial glycosidation of avermectins at the 14a-position
INVENTOR(S): Arison, Byron H.; Schulman, Marvin D.; Young, Noel M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 524687 | A1 | 19930127 | EP 1992-202163 | 19920715 |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| CA 2074327 | AA | 19930124 | CA 1992-2074327 | 19920721 |
| AU 9220469 | A1 | 19930311 | AU 1992-20469 | 19920722 |
| AU 646749 | B2 | 19940303 | | |
| ZA 9205508 | A | 19930331 | ZA 1992-5508 | 19920722 |
| JP 06049090 | A2 | 19940222 | JP 1992-196652 | 19920723 |

PRIORITY APPLN. INFO.: US 1991-734395 19910723
OTHER SOURCE(S): MARPAT 118:167616
AB Avermectins are glycosidated at the 14a position using Bacillus subtilis ATCC 55060. The commonest group added is glucosyl. The glycosides are

useful as plant and animal parasiticides (no data). The glycosidation of a no. of aglycons is demonstrated.

L52 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 1993:408566 CAPLUS
DOCUMENT NUMBER: 119:8566
TITLE: A novel fragmentation reaction of avermectin aglycones
AUTHOR(S): Blizzard, Timothy A.; Margiatto, Gaye M.; Mrozik, Helmut; Fisher, Michael H.
CORPORATE SOURCE: Merck Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Journal of Organic Chemistry (1993), 58(11), 3201-3
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB An unexpected fragmentation reaction of ***avermectin*** ***aglycons*** was discovered during the course of synthetic studies directed toward 13-epi-avermectins. Aglycon I cleanly and rapidly affords fragmentation product II in the presence of $AgClO_4$ and $SnCl_2$ in ether. The effects of various reaction conditions and structure modifications on the fragmentation reaction are described. Structure elucidation and bioactivity of II are discussed briefly.

L52 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:538959 CAPLUS
DOCUMENT NUMBER: 119:138959
TITLE: Inversion of the sterically constrained C13-hydroxyl of 22,23-dihydroavermectin B1 aglycone
AUTHOR(S): Senanayake, Chris H.; Singh, Sheo B.; Bill, Timothy J.; DiMichele, Lisa M.; Liu, Ji; Larsen, Robert D.; Verhoeven, Thomas R.
CORPORATE SOURCE: Dep. Process Res., Merck Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Tetrahedron Letters (1993), 34(15), 2425-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 119:138959
GI

/ Structure 2 in file .gra /

AB The development of novel, mild inversion chem. which facilitates the prepn. of the 13-epi-22,23-dihydroavermectin B1 aglycon (I) is discussed.

L52 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:254627 CAPLUS
DOCUMENT NUMBER: 118:254627
TITLE: Procedure for the inversion of the stereochemistry at C13 of ***avermectin*** ***aglycon*** compounds
INVENTOR(S): Jones, Todd K.; Mrozik, Helmut
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 514090 | A1 | 19921119 | EP 1992-304151 | 19920508 |

R: CH, DE, FR, GB, IT, LI, NL

| | | | | |
|---|---|---|---|---|
| CA 2068388 | AA | 19921114 | CA 1992-2068388 | 19920511 |
| AU 9216200 | A1 | 19921119 | AU 1992-16200 | 19920512 |
| ZA 9203421 | A | 19921230 | ZA 1992-3421 | 19920512 |
| JP 05163276 | A2 | 19930629 | JP 1992-120193 | 19920513 |

PRIORITY APPLN. INFO.: US 1991-698874 19910513
OTHER SOURCE(S): CASREACT 118:254627; MARPAT 118:254627
GI

/ Structure 3 in file .gra /

AB ***Avermectin*** ***aglycons*** I (R = H, OH, :O; R1 = alkyl, alkenyl, cycloalkyl; R2 = OH, alkoxy, :O, :NOH; R3 = H; R4 = OH) and their 22,23-didehydro analogs were inverted at C-13 by acylation, treatment with a tetraalkylammonium nitrate, and denitration with Zn-AcOH. Thus, I (R = .alpha.-OH, R1 = CHMeEt, R2 = OSiMe2CMe3, R3 = H, R4 = OH, II) was converted to II (R4 = tosyloxy) which was treated with Bu4N NO3 to give II (R3 = ONO2, R4 = H). Treatment of this compd. with Zn-AcOH gave II (R3 = OH, R4 = H).

L52 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:510104 CAPLUS
DOCUMENT NUMBER: 117:110104
TITLE: 5.beta.- and 13.beta.-ivermectin monoglucopyranoside preparation with Bacillus
INVENTOR(S): Arison, Byron H.; Petuch, Brian R.; Chen, Shieh Shung Tom; Inamine, Edward S.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 481672 | A1 | 19920422 | EP 1991-309297 | 19911009 |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| AU 9185831 | A1 | 19920416 | AU 1991-85831 | 19911014 |
| ZA 9108158 | A | 19920624 | ZA 1991-8158 | 19911014 |
| CA 2053432 | AA | 19920416 | CA 1991-2053432 | 19911015 |
| JP 06065279 | A2 | 19940308 | JP 1991-266463 | 19911015 |

PRIORITY APPLN. INFO.: US 1990-597654 19901015
AB The ivermectins 5.beta.- and 13.beta.-ivermectin monoglucopyranoside are prepd. from 13-.beta.-hydroxy- ***avermectin*** ***aglycon*** with a novel isolate of Bacillus subtilis. 13.beta.-Ivermectin monoglucopyranoside is the major product. The novel compds. can be used to treat parasitic infections in mammals (no data). B. subtilis ATCC 55060 was cultured in Soy Glucose medium contg. 13-.beta.-hydroxy ***avermectin*** ***aglycon*** 50 .mu.g/mL at 27.degree. for 18 h to yield these two compds.

L52 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:150145 CAPLUS
DOCUMENT NUMBER: 116:150145
TITLE: Glycosylation of avermectin aglycones with Streptomyces avermitilis mutants
INVENTOR(S): Omstead, Mary Nallin; Schulman, Marvin D.; Young, Noel M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 463677 | A2 | 19920102 | EP 1991-201493 | 19910614 |
| EP 463677 | A3 | 19920429 | | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| CA 2044875 | AA | 19911223 | CA 1991-2044875 | 19910618 |
| JP 04252192 | A2 | 19920908 | JP 1991-148932 | 19910620 |
| AU 9179265 | A1 | 19920102 | AU 1991-79265 | 19910621 |
| ZA 9104790 | A | 19920527 | ZA 1991-4790 | 19910621 |
| US 5188944 | A | 19930223 | US 1991-762183 | 19910919 |

PRIORITY APPLN. INFO.: US 1990-542343 19900622
OTHER SOURCE(S): MARPAT 116:150145
GI

/ Structure 4 in file .gra /

AB ***Avermectin*** ***aglycons*** are glycosidated using S. avermitilis isolates that do not produce avermectins. The microorganism adds .alpha.-L-oleandrose groups to the aglycons to give I (R1=H,Me; R2=H, methoxy keto, acetyl; R3= H, OH, double bond at dashed line; n=0,1). The prepn. of the oleandrosides, with methylation of the 5-hydroxyl group in some cases, is demonstrated.

L52 ANSWER 15 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 92:632232 SCISEARCH
THE GENUINE ARTICLE: JU801
TITLE: SYNTHESIS AND BIOLOGICAL-ACTIVITY OF 13-EPI-AVERMECTINS - POTENT ANTHELMINTIC AGENTS WITH AN INCREASED MARGIN OF SAFETY
AUTHOR: BLIZZARD T A (Reprint); MARGIATTO G M; MROZIK H; SHOOP W L; FRANKSHUN R A; FISHER M H
CORPORATE SOURCE: MERCK SHARP & DOHME LTD, R50G-231, POB 2000, RAHWAY, NJ, 07065 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (16 OCT 1992) Vol. 35, No. 21, pp. 3873-3878.
ISSN: 0022-2623.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 28
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Chemical conversion of the potent anthelmintic natural products avermectin B1 (1) and avermectin B2 (3) to the corresponding 13-epi analogs (15 and 9) is described. The novel analogs retain the full potency of the natural products but are substantially safer.

L52 ANSWER 16 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 93:32211 SCISEARCH
THE GENUINE ARTICLE: KF709
TITLE: 13-BETA-HYDROXYLATION OF MILBEMYCINS BY SELENIUM DIOXIDE
AUTHOR: TSUKAMOTO Y (Reprint); SATO K; KINOTO T; YANAI T
CORPORATE SOURCE: SANKYO CO LTD, AGR CHEM RES LABS, 1041 YASU, YASU, SHIGA 52023, JAPAN (Reprint)
COUNTRY OF AUTHOR: JAPAN
SOURCE: BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, (DEC 1992) Vol. 65, No. 12, pp. 3300-3307.
ISSN: 0009-2673.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: ENGLISH
REFERENCE COUNT: 30
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Introduction of a hydroxyl group to milbemycin nucleus was examined. Starting from 5-oxo-5-deoxy-milbemycins, 13beta-hydroxy-5-oxo-5-deoxymilbemycins were obtained stereo- and regioselectively by selenium

dioxide oxidation in formic acid and subsequent acidic hydrolysis. The stereochemistry of the hydroxyl group was elucidated by H-1 NMR study.

L52 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:151394 CAPLUS
DOCUMENT NUMBER: 116:151394
TITLE: Total synthesis of 22,23-dihydroavermectin B1b aglycon
AUTHOR(S): Ferezou, Jean Pierre; Julia, Marc; Liu, Lu Wei; Pancrazi, Ange
CORPORATE SOURCE: Lab. Chim., Ec. Norm. Super., Paris, 75231, Fr.
SOURCE: Bulletin des Societes Chimiques Belges (1992), 101(1), 65-6
CODEN: BSCBAG; ISSN: 0037-9646
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A lecture with no refs.

L52 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:492732 CAPLUS
DOCUMENT NUMBER: 115:92732
TITLE: Total synthesis of the anthelmintic macrolide avermectin B1a
AUTHOR(S): Ley, Steven V.; Armstrong, Alan; Diez-Martin, David; Ford, Mark J.; Grice, Peter; Knight, Julian G.; Kolb, Hartmuth C.; Madin, Andrew; Marby Craig A.; et al.
CORPORATE SOURCE: Dep. Chem., Imp. Coll. Sci. Technol. Med., London, SW7 2AY, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1991), (4), 667-92
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:92732
GI

/ Structure 5 in file .gra /

AB A highly convergent total synthesis of the anthelmintic macrolide avermectin B1a is described. The key features of this synthesis include the introduction of the C(11)-C(15) portion by selective ring opening of a sym. 1,4-bis-epoxide I followed by reaction with the anion derived from the phenylsulfonypyran II to afford the northern C(11)-C(25) fragment. Coupling of the derived C(11)-C(25) aldehyde unit III (R = SiMe2CMe3) with a C(1)-C(10) southern fragment IV was achieved via a novel deconjugative vinyl sulfone anion sequence. Macrolactonization and subsequent introduction of the 3,4-double bondgave the aglycon portion. The oleandrosyloleandrose disaccharide was introduced by a novel Ag-mediated coupling between the 5-acetylated aglycon and the thiocarbonylimidazolide of the disaccharide.

L52 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:206852 CAPLUS
DOCUMENT NUMBER: 114:206852
TITLE: Model studies of palladium-catalyzed coupling reactions for the "south-north" attachment of avermectins
AUTHOR(S): Ferezou, Jean Pierre; Julia, Marc; Li, Yun; Liu, Lu Wei; Pancrazi, Ange
CORPORATE SOURCE: Lab. Chim., Ec. Norm. Super., Paris, F-75231, Fr.
SOURCE: Synlett (1991), (1), 53-6
CODEN: SYNLES; ISSN: 0936-5214
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:206852
GI

/ Structure 6 in file .gra /

AB Model Pd-catalyzed vinyl-vinyl coupling reactions have been tested for the construction of the 8E,10E-diene system of avermectins. Cross coupling of the southern bicyclic vinyl iodide I, prepd. from Et 2-oxocyclohexanecarboxylate, with northern 1-alkenylstannanes or the one-carbon-homologation reagent tributyl(4-methoxybenzyloxymethyl)stannane occurs with acceptable yields.

L52 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:81431 CAPLUS
DOCUMENT NUMBER: 114:81431
TITLE: Avermectin ketal derivatives useful as antiparasitic agents
INVENTOR(S): Blizzard, Timothy A.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 388019 | A1 | 19900919 | EP 1990-301638 | 19900215 |
| EP 388019 | B1 | 19940427 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE | | | | |
| CA 2010078 | AA | 19900816 | CA 1990-2010078 | 19900214 |
| ZA 9001148 | A | 19901031 | ZA 1990-1148 | 19900215 |
| AU 9049830 | A1 | 19910829 | AU 1990-49830 | 19900215 |
| AU 623744 | B2 | 19920521 | | |
| AT 104983 | E | 19940515 | AT 1990-301638 | 19900215 |
| ES 2063256 | T3 | 19950101 | ES 1990-301638 | 19900215 |
| JP 02270880 | A2 | 19901105 | JP 1990-34038 | 19900216 |
| US 5077308 | A | 19911231 | US 1990-556044 | 19900723 |

PRIORITY APPLN. INFO.: US 1989-311268 19890216
EP 1990-301638 19900215
OTHER SOURCE(S): MARPAT 114:81431
GI

/ Structure 7 in file .gra /

AB The title compds. (I; R1 = H, OH; R2 = alkyl, alkenyl; X = Q1, Q2; Y = Q3, Q4; dotted line = optional bond; R3 = alkyl, Ph, alkoxyalkyl, haloalkyl, alkenyl, alkynyl; R4 = H, alkyl; n = 2, 3), were prepd. for treatment/prevention of parasitic infections in animals and for combating plant pests (no data). Thus, Me3CSiMe2Cl, 22,23-dihydroavermectin B1 aglycon, imidazole, and DMF were stirred 22 h to give 5-O-tert-butyldimethylsilyl-22,23-dihydroavermectin B1 aglycon. The latter was oxidized to the 13-oxo deriv. with Me2SO/(COCl)2 in CH2Cl2 at -78.degree. followed by desilylation with H2O/4-MeC6H4SO3H/MeOH and ketalization with HOCH2CH2OH, 2-methoxy-1,3-dioxolane, and BF3.Et2O in PhMe at room temp. to give 13-oxo-13-deoxy-22,23-dihydroavermectin B1 aglycon 13-ethylene ketal.

L52 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:478894 CAPLUS
DOCUMENT NUMBER: 113:78894
TITLE: Preparation of alkylavermectin derivatives as antiparasitic, anthelmintic, and pesticidal agents
INVENTOR(S): Eskola, Philip; Shin, Thomas L.; Mrozik, Helmmut
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 351923 | A2 | 19900124 | EP 1989-201897 | 19890719 |
| EP 351923 | A3 | 19910313 | | |
| EP 351923 | B1 | 19951220 | | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| US 4906619 | A | 19900306 | US 1988-222868 | 19880722 |
| AU 8938851 | A1 | 19900125 | AU 1989-38851 | 19890721 |
| AU 606292 | B2 | 19910131 | | |
| JP 02078683 | A2 | 19900319 | JP 1989-190420 | 19890721 |
| ZA 8905566 | A | 19900425 | ZA 1989-5566 | 19890721 |

PRIORITY APPLN. INFO.: US 1988-222868 19880722
OTHER SOURCE(S): MARPAT 113:78894
GI

/ Structure 8 in file .gra /

AB The title compds. [I; A, B = single or double bond; when R1 = OH, R2 = (substituted) lower alkyl, lower cycloalkyl, lower alkenyl; when R1 = H, R2 = OH or OMe; when A = double bond, R4 = absent and R3 = H or lower alkyl; when A = single bond, R3 = OH and R4 = any one of the groups listed in R2; when R5 = OH, R6 = any one of the groups listed in R2; or when R5 = H, R6 = H, halo, OH, Q,, Q1; when R7 = OH, R8 = any one of the groups listed in R2; or when R7 = H, R8 = OH, substituted NH2; when B = single bond, R9 = OH and R10 = any one of the groups listed in R2; or R9 = H, R10 = H, OH; when B = double bond, R10 = absent and R9 = H; R11 = Me, Et, Me2CH, Me2CHCH2, CMe:CHMe, CMe:CHEt, CMe:CHCHMe2; provided that, e.g. when at the disubstituted positions 5, 10, 13, 23, 4', and 4'', at least one of R1, R3, R5, R7, and R9 = OH and the corresponding R2, R4, R6, R8, and R10 = any one of the groups listed in R2] useful as antiparasitic, anthelmintic, and pesticidal agents (no data), are prepd. by reaction of an avermectin compd. having a ketone group at one or more of positions 5, 10, 13, 23, 4', or 4'', with RMgX (R = any one of the groups listed in R2, X = halo). Thus, 0.5 mL 2.85 M MeMgBr in Et2O was added to a stirred soln. of 23-oxoavermectin B2a/B2b (prepn. given) in THF and the stirring was continued 1 h to give 23-methylavermectin B2a/B2b.

L52 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:2292 CAPLUS
DOCUMENT NUMBER: 114:2292
TITLE: Purification and identification of dTDP-oleandrose, the precursor of the oleandrose units of the avermectins
AUTHOR(S): Schulman, Marvin D.; Acton, Susan L.; Valentino, Delia L.; Arison, Byron H.
CORPORATE SOURCE: Dep. Fermentation Microbiol., Merck Sharpe and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Journal of Biological Chemistry (1990), 265(28), 16965-70
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The nucleotide sugar precursor of the oleandrose units of the avermectins has been purified from a mutant of Streptomyces avermitilis, which does not synthesize any avermectins but which converts ***avermectin*** ***aglycons*** to their resp. disaccharides. This precursor has been identified as dTDP-oleandrose. The purifn. was achieved by anion exchange and reverse phase HPLC. The purified nucleotide sugar had an absorption spectra characteristic of thymidine, released dTMP when treated with phosphodiesterase, and possessed an NMR spectrum in which 3 resonances characteristic of oleandrose were seen in addn. to the thymidine signals. The enzyme, ***avermectin*** ***aglycon*** dTDP-oleandrose glycosyltransferase, which catalyzes the stepwise addn. of oleandrose to the ***avermectin*** ***aglycons*** , has been demonstrated in cell-free exts. and (NH4)2SO4 fractions of cell-free exts. of S.

avermitilis. The enzyme is specific for dTDP-oleandrose as the glycosyl donor but utilizes all ***avermectin*** ***aglycons*** as glycosyl acceptors. The stoichiometry between dTDP-oleandrose consumed in the reaction and oleandrose units transferred to the avermectin mono- and disaccharide was found to be 1:1.

L52 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:98270 CAPLUS
DOCUMENT NUMBER: 112:98270
TITLE: Synthesis of avermectin B1a aglycon
AUTHOR(S): White, James D.; Bolton, Gary L.
CORPORATE SOURCE: Dep. Chem., Oregon State Univ., Corvallis, OR, 97331-4003, USA
SOURCE: Journal of the American Chemical Society (1990), 112(4), 1626-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:98270
GI

/ Structure 9 in file .gra /

AB A convergent total synthesis of the aglycon of avermectin B1a was completed via Julia coupling of sulfone I with the oxahydrindenone II (R = OSiEt3). I was prepd. from a previously synthesized spiroketal intermediate, whereas II (R = OSiEt3) was obtained by angular hydroxylation of II (R = H), acquired earlier by synthesis. A reductive elimination of the resulting sulfone lactone established the E,E-diene system of the aglycon.

L52 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:75304 CAPLUS
DOCUMENT NUMBER: 112:75304
TITLE: Production of avermectin aglycones by strains of Streptomyces avermitilis
INVENTOR(S): Lam, Lapyuen Harry; Wax, Richard Gerald; McArthur, Hamish Alastair Irvine
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 313297 | A2 | 19890426 | EP 1988-309724 | 19881017 |
| EP 313297 | A3 | 19900725 | | |
| EP 313297 | B1 | 19930519 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| AT 89604 | E | 19930615 | AT 1988-309724 | 19881017 |
| ES 2054822 | T3 | 19940816 | ES 1988-309724 | 19881017 |
| DK 8805869 | A | 19890614 | DK 1988-5869 | 19881021 |
| JP 01153083 | A2 | 19890615 | JP 1988-265943 | 19881021 |
| JP 06104058 | B4 | 19941221 | | |
| CA 1337757 | A1 | 19951219 | CA 1988-580988 | 19881021 |
| US 5240850 | A | 19930831 | US 1991-660972 | 19910226 |
| US 5576200 | A | 19961119 | US 1994-323479 | 19941014 |
| US 5583029 | A | 19961210 | US 1994-323247 | 19941014 |

PRIORITY APPLN. INFO.: US 1987-112972 19871023
EP 1988-309724 19881017
US 1991-660972 19910226
US 1993-60451 19930511
US 1993-60942 19930511
OTHER SOURCE(S): MARPAT 112:75304

GI

/ Structure 10 in file .gra /

AB ***Avermectin*** ***aglycons*** [(I), R1 = OH when double bond is absent; R2 = 4-(.alpha.-L-oleandrosyl)-.alpha.-L-oleandrosyloxy (II), R3 = H, Me; R4 = .alpha.-branched alkyl, cycloalkyl, etc.] useful as parasiticides, are manufd. by fermn. of strains of Streptomyces avermitilis that lack branched-chain 2-oxoacid dehydrogenase, in addn. to being unable to glycosylate compds. I, in the presence of suitable branched-chain carboxylic acids or precursors thereof. A suitable strain of S. avermitilis was produced by mutagenesis and fermn. with cyclopentane carboxylic acid 11 g to yield 9 mg of 25-cyclopentenylavermectin A2 aglycon (I; R = OH; double bond is absent, R2 = cyclopentenyl, R3 = Me, R4 = OH).

L52 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:228309 CAPLUS
DOCUMENT NUMBER: 110:228309
TITLE: Studies on the biosynthesis of avermectins
AUTHOR(S): Chen, Tom S.; Inamine, Edward S.
CORPORATE SOURCE: Dep. Ferment. Microbiol., Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Archives of Biochemistry and Biophysics (1989), 270(2), 521-5
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To elucidate the pathway of avermectin biosynthesis, the biosynthetic relationships of avermectins A1a, A2a, B1a, B2a, and their resp. monosaccharides and aglycons were studied. 14C-labeled avermectin compds. prepd. from [1-14C]acetate were fed to Streptomyces avermitilis strain MA5502 and their metabolites were detd. Two furan ring-free aglycons, 6,8a-seco-6,8a-deoxy-5-keto avermectin B1a and B2a, have been isolated from the fermn. broth of a blocked mutant of S. avermitilis. Addn. of the compds. and a semisynthetic compd., 5-keto avermectin B2a aglycon, to the fermn. medium of a second blocked mutant established that the two compds. are intermediates in the avermectin biosynthetic pathway immediately preceding ***avermectin*** ***aglycons*** .

L52 ANSWER 26 OF 38 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 89110921 MEDLINE
DOCUMENT NUMBER: 89110921 PubMed ID: 2913297
TITLE: Syntheses and biological activities of 13-substituted ***avermectin*** ***aglycons*** .
AUTHOR: Mrozik H; Linn B O; Eskola P; Lusi A; Matzuk A; Preiser F A; Ostlind D A; Schaeffer J M; Fisher M H
CORPORATE SOURCE: Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., Rahway, New Jersey 07065.
SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (1989 Feb) 32 (2) 375-81.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198903
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890308
AB The reactions of sulfonate esters of the allylic/homoallylic 13-alcohol of 5-O-(tert-butyldimethylsilyl)-22,23-dihydroavermectin B1a aglycon (1a) were investigated. Nucleophilic substitution gave 13 beta-chloro and 13 beta-iodo derivatives, while solvolytic reaction conditions yielded 13 alpha-methoxy, 13 alpha-fluoro, and 13 alpha-chloro products. A mixture of 13 alpha- and 13 beta-fluorides was obtained upon reaction with DAST. The 13 beta-iodide gave, upon elimination with lutidine, the 8(9),10(11),12(13),14(15)-tetraene. The 13 beta-alcohol and the

rearranged 15-ol 13(14)-ene and 15-amino 13(14)-ene derivatives were obtained by substitution via the allylic carbonium ion. MEM ethers 11 and 12 of the two epimeric 13-ols were prepared by alkylation with MEM chloride. In contrast, methylation of 1a with MeI and Ag2O in CH2Cl2 occurred exclusively at the tertiary 7-hydroxy group and not at the secondary 13 alpha-ol. Oxidation of the allylic alcohol 1a proceeded under Swern conditions but not with MnO2 to the 13-oxo aglycon, which was reduced by NaBH4 exclusively to the natural 13 alpha-ol, while reductive amination with NaCNBH3-NH4OAc gave the 13 alpha-amine. The methoxime derivative was obtained in the form of the two geometric isomers. Anthelmintic activities against the sheep nematode Trichostrongylus colubriformis, miticidal activities against the two-spotted spider mite (Tetranychus urticae), and insecticidal activities against the southern armyworm (Spodoptera eridania) as well as the binding constants to a free living nematode (Caenorhabditis elegans) derived receptor assay were obtained and compared to avermectin B1a, 22,23-dihydroavermectin B1a, and the 13-deoxy-22,23-dihydroavermectin B1 aglycon related to the milbemycins. None of the newly prepared derivatives exceeded the potency of the three reference compounds. Lipophilic 13-substituents such as halogen, alkoxy, and methoxime retained high biological activities in all assays, while the more polar substituents hydroxy and amino had weaker activities. Rearranged 15-substituted 13(14)-ene derivatives were completely inactive. The 13-oxo and the 12,13-dehydro analogues were only weakly active in vivo despite having good binding affinity to the receptor, possibly due to instability or poor absorption.

L52 ANSWER 27 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 89:81274 SCISEARCH
THE GENUINE ARTICLE: T0491
TITLE: SYNTHESES AND BIOLOGICAL-ACTIVITIES OF 13-SUBSTITUTED ***AVERMECTIN*** ***AGLYCONS***
AUTHOR: MROZIK H (Reprint); LINN B O; ESKOLA P; LUSI A; MATZUK A; PREISER F A; OSTLIND D A; SCHAEFFER J M; FISHER M H
CORPORATE SOURCE: MERCK SHARP & DOHME RES LABS, POB 2000, RAHWAY, NJ, 07065 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (1989) Vol. 32, No. 2, pp. 375-381.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 11

L52 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:55728 CAPLUS
DOCUMENT NUMBER: 108:55728
TITLE: The total synthesis of the aglycon of avermectin A1a
AUTHOR(S): Danishefsky, Samuel J.; Armistead, David M.; Wincott, Francine E.; Selnick, Harold G.; Hungate, Randall
CORPORATE SOURCE: Dep. Chem., Yale Univ., New Haven, CT, 06511, USA
SOURCE: Journal of the American Chemical Society (1987), 109(26), 8117-19
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:55728
GI

/ Structure 11 in file .gra /

AB A total synthesis of the aglycon I of avermectin A1a was achieved. D-Glucose and D-ribose were used as building blocks to create the subunits required for a synthesis of avermectin A1a aglycon in chirally matched form. The key steps involved an aldol reaction to join the subunits, an intramol. Nozaki reaction, a Mukaiyama macrolactonization, and a deconjugation of a .DELTA.2 system to the naturally occurring .DELTA.3 series. The stereochem. is controlled through equilibration and recycling.

L52 ANSWER 29 OF 38 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 88058774 MEDLINE
DOCUMENT NUMBER: 88058774 PubMed ID: 3680172
TITLE: Genetic studies of avermectin biosynthesis in Streptomyces avermitilis.
AUTHOR: Ikeda H; Kotaki H; Omura S
CORPORATE SOURCE: School of Pharmaceutical Sciences, Kitasato University, Tokyo, Japan.
SOURCE: JOURNAL OF BACTERIOLOGY, (1987 Dec) 169 (12) 5615-21. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198801
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19880114

AB A genetic recombination study of an industrial strain of Streptomyces avermitilis which produces avermectin is described. A genetic map has been constructed by analysis of haploid recombinants and linkage relationships of 16 marker loci. Fifteen avermectin-nonproducing mutants, produced by mutagenesis, were classified into two phenotypically different groups, of which one produced ***avermectin*** ***aglycon*** and the other was able to convert ***avermectin*** ***aglycon*** to avermectins. Two different mutants were found to map closely to each other.

L52 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:167168 CAPLUS
DOCUMENT NUMBER: 108:167168
TITLE: A novel degradation in the avermectin series: a stereospecific osmylation reaction
AUTHOR(S): Selnick, Harold G.; Danishefsky, Samuel J.
CORPORATE SOURCE: Dep. Chem., Yale Univ., New Haven, CT, 06511, USA
SOURCE: Tetrahedron Letters (1987), 28(42), 4955-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:167168
GI

/ Structure 12 in file .gra /

AB The reaction of OsO4 on the conjugated isomer I (RR1 = bond) of ***avermectin*** ***aglycon*** , occurs with high regio and facial selectivity, giving I (R = R1 = OH) which was oxidatively cleaved to spiroketal and benzofuran fragments by Pb(OAc)4.

L52 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:514842 CAPLUS
DOCUMENT NUMBER: 105:114842
TITLE: Substituted and unsubstituted 13-(alkoxy)methoxy derivatives of the avermectin aglycones, compositions and use
INVENTOR(S): Linn, Bruce O.; Mrozik, Helmut H.
PATENT ASSIGNEE(S): Merck and Co., Inc. , USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4587247 | A | 19860506 | US 1985-705254 | 19850225 |
| EP 193347 | A2 | 19860903 | EP 1986-301168 | 19860219 |
| EP 193347 | A3 | 19861029 | | |

| | | | | |
|---|---|---|---|---|
| EP 193347 | B1 | 19900829 | | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| AU 8654004 | A1 | 19860828 | AU 1986-54004 | 19860224 |
| AU 574566 | B2 | 19880707 | | |
| ZA 8601351 | A | 19861029 | ZA 1986-1351 | 19860224 |
| JP 61200993 | A2 | 19860905 | JP 1986-38455 | 19860225 |
| JP 2509560 | B2 | 19960619 | | |
| JP 08073466 | A2 | 19960319 | JP 1995-220965 | 19950830 |
| JP 2647361 | B2 | 19970827 | | |

PRIORITY APPLN. INFO.: US 1985-705254 19850225
GI

/ Structure 13 in file .gra /

AB The title compds. I (R1 = H, OH; R2 = C1-4 alkyl; R4 = X(CH2)nOCH2O; X = H, C1-6 alkyl, alkoxy, Ph, heterocyclyl, etc.; n = 1-6) useful as anthelmintic, insecticide and pesticide (no data) were prepd. Thus, 13-O-methoxymethyl-5-O-tert-butyldimethylsilyl-22,23-dihydroavermectin B1a aglycon prepd. by reaction of ClCH2OMe with 5-O-butyldimethylsilyl-22,23-dihydroavermectin B1a aglycon and MeCH2N(CHMe2)2 in CH2Cl2, was treated with 4-MeC6H4SO3H to give 13-O-methoxymethyl-22,23-dihydroavermectin B1a aglycon.

L52 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:31378 CAPLUS
DOCUMENT NUMBER: 106:31378
TITLE: Avermectin bioconversion products
INVENTOR(S): Goegelman, Robert T.; White, Raymond F.; Inamine, Edward S.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 72 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 194125 | A2 | 19860910 | EP 1986-301494 | 19860303 |
| EP 194125 | A3 | 19861029 | | |
| EP 194125 | B1 | 19920212 | | |
| R: CH, DE, FR, GB, IT, LI, NL | | | | |
| US 4666937 | A | 19870519 | US 1986-830333 | 19860220 |
| ZA 8601553 | A | 19861029 | ZA 1986-1553 | 19860303 |
| AU 8654265 | A1 | 19860911 | AU 1986-54265 | 19860304 |
| AU 582833 | B2 | 19890413 | | |
| JP 61233686 | A2 | 19861017 | JP 1986-45488 | 19860304 |

PRIORITY APPLN. INFO.: US 1985-708194 19850304
GI

/ Structure 14 in file .gra /

AB The title compds. (I; R1-R7 = H, OH; R8 = H, epi-OH) were isolated from (Cunninghamella blakesleena (ATCC 8688a) cultures incubated, with ***avermectin*** ***aglycons*** as antiparasitic, insecticidal, and anthelmintic agents. Thus, C. blakesleena MF-4415, ATCC 8688a was seed cultured with dextrose, nutrient broth, and yeast, and malt exts., inoculated onto slats and finally incubated with 22, 23-dihydroavermectin B1a aglycon. The CH2Cl2 ext. of whole broth gave 4 I after reverse phase column chromatog.

L52 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:608623 CAPLUS
DOCUMENT NUMBER: 105:208623